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NOTICE

As the result of an error in pagination, pages 65 to 72 inclusive were omitted from Volume 60 of THE BULLETIN OF THE JOHNS HOPKINS HOSPITAL. The omission occurred between the January and February, 1937 numbers.

A STUDY OF FOUR CATS DEPRIVED OF NEOCORTEX AND ADDITIONAL PORTIONS OF THE FOREBRAIN*

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Submitted for publication November 20, 1936

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INTRODUCTION

The studies of Goltz (16) and of Rothmann (33) on dogs, and of Dusser de Barenne (12) on cats, have provided excellent descriptions

* This investigation has been aided by a grant from the Josiah Macy, Jr. Foundation.

of the general behavior and of many specific reactions of carnivores which have long survived removal of the cerebral cortex. A desire on the part of one of us to investigate the neural bases for the display of certain forms of emotional excitement led to the preparation of a number of cats in which forebrain ablations differing in extent had been carried out. Four of these chronic preparations form the basis of this report. Histological studies of their brains showed that in each case the bilateral ablations were very nearly symmetrical and that in the different animals there had been removed, in addition to neocortex, different amounts of paleocortex, archicortex and brain stem.[1] We have, therefore, been able to draw certain conclusions as to the rôles played by the remaining parts of the brain in the elaboration of the behavior of the cat without neocortex.

In the present report considerable attention has been devoted to emotional expression.[2] The ease with which signs of anger could be elicited in their preparations was noted by all who have studied chronically decorticate dogs and cats. It appeared worthwhile to investigate this capacity in greater detail. Furthermore, it seemed reasonable to suppose that, if after decortication a reaction pattern such as that of rage could be elicited, certain other forms of emotional expression might also be evoked. One might, for example, expect to obtain evidence that the neural mechanisms essentially concerned in the expression of fear and sexual excitement remain after decortication. No indication that such is the case had been given in the reports of earlier investigators. We therefore consider it a point of

[1] In this paper *cortex* or *pallium* is used to describe the cerebral cortex as a whole. *Neocortex* or *neopallium* refers to the so-called non-olfactory or somatic cortex; it lies dorsal to the rhinal fissure. The rest of the cortex, composed largely of the hippocampus and pyriform lobe, may be divided into *archicortex* and *paleocortex*. These phylogenetically older subdivisions are commonly termed olfactory cortex, although they doubtless subserve certain non-olfactory functions. They have therefore been classified as cortical portions of the rhinencephalon and in our anatomical descriptions they are considered as parts of that division of the brain.

[2] A recent review (4) of the subject of emotional expression after decortication includes a somewhat abbreviated account of the four cats described in this paper and considers their emotional behavior in relation to other experimental findings and to certain theoretical views.

some interest that our observations showed that the decorticate cat is capable of displaying definite signs of fear. This investigation has also provided an instance of the occurrence of typical oestrual behavior in a cat from which all neocortex and some additional forebrain tissue had been removed.

The advantages of becoming thoroughly familiar with the normal responses and behavior of any animal which is to be studied during a long postoperative survival period are obvious. We wish to emphasize that this was done in the case of the four subjects of this report and to point out that there were some marked differences in the preoperative "temperaments" and general character of these animals.

The changes in behavior and response which occur during the first days following total decortication have been noted by several writers. The problems raised by these phenomena involve questions of "compensation," "learning," "irritation," etc., which should be separately examined and do not fall within the scope of this paper. Hence, except for occasional observations which are of particular interest, this report is only concerned with a description and discussion of the reactions and behavior of our preparations after they had arrived at an essentially steady state.

I. PREPARATION AND GENERAL DESCRIPTION OF THE ANIMALS

(1) *Cat 103*

This was a small mature female that had been kept under observation for nine months before the first intracranial operation was performed. During that time she showed herself to be an alert, clean, gentle and very friendly animal. From the first she sought, obtained and enjoyed much petting. She always purred when stroked and could be handled quite roughly without exhibiting rage or fear. She showed signs of anger only when some nociceptive stimulus was applied or when she was restrained in some unusual position. In contrast to her friendly attitude toward human beings she usually displayed resentment when approached by another cat of either sex. Early in this observation period (in November, 1928) a supposedly complete bilateral ovariectomy was performed. At autopsy in April, 1932, however, a small fragment of ovarian tissue was found

and, on the basis of the oestrual behavior described below, it is certain that this had been functionally active.

The object of the first intracranial operation,[3] carried out July 5, 1929, was the removal of all neocortex of the right hemisphere. After a rapid and uneventful recovery the animal exhibited, during the five and one-half months which elapsed between the first and second cerebral ablations, the same traits which had characterized her behavior during the preoperative observation period. In the light of a study of some forty hemidecorticate cats it can be stated that unilateral removal of neocortex or ablation of all cortex and most of the striatum on one side does not ostensibly alter the individual peculiarities of the animal. The easily detectable deficiencies of such cats are limited to: a nearly total blindness of the eye opposite the ablation, hypesthesia of the contralateral half of the body and a deficiency of certain postural reactions of the contralateral legs (3). These legs also exhibit as a permanent result of the ablation an extensor rigidity which is clearly manifested only when the animal is suspended.

Removal of the remaining (the left) neocortex of cat 103 was carried out December 23, 1929. On the third postoperative day, just after complete emergence from the anesthetic (sodium barbital), she began to walk and two days later she took food of her own accord when her mouth was brought into contact with it. From that time forth her general behavior was remarkably constant. Except for two or three periods of diarrhea her health remained good up to the latter part of 1931, when she developed an ever increasing tendency to bite herself in response to the slightest cutaneous irritation. Because of the severity of many of the wounds thus inflicted she was killed in April, 1932, two years and four months after the second and final cerebral ablation. Her brain (Fig. 21) was at once removed and prepared for histological examination.

The brain was sectioned serially at 40 μ and stained by the Weigert-Pal method. Every fifth section was mounted. A summary of the histological examination with regard to the nuclear configuration is given below. A graphic representation summarizing the extent of the ablations and the secondary degenerations is given in Fig. 25.

[3] The surgical methods employed in this work have been described elsewhere (3) and need not be repeated here.

Certain of the fiber connections will be considered in the appendix (p. 119).

Neopallium. On the left the neopallium had been entirely removed. On the right there was a small portion of the gyrus splenius posterior attached to the caudal margin of the gyrus hippocampi.

Rhinencephalon. The olfactory bulbs and stalks were present, but the stalks had been injured along their dorsolateral margins, the left more than the right. The left lateral olfactory stria was cut at the level of the rostral pole of the tuberculum olfactorium. The tuberculum olfactorium was damaged along its lateral margin on the left, but was intact on the right (Tub. ol., Fig. 1). The septal nuclei were greatly shrunken, although not directly involved in the lesion (N. p-ol. m. and l, Fig. 1). The diagonal band of Broca and its nucleus (Diag. B, Fig. 1) and also the nucleus accumbens (N. ac., Fig. 1) appeared normal on both sides, but the bed nuclei of the anterior commissure and of the stria terminalis (N. st. t., Figs. 1, 2) were reduced in size. The interbulbar component of the anterior commissure was essentially unchanged (T. ol. m., Fig. 1), but the posterior component was degenerated, having been cut at the lateral margin of the putamen on the right. On the left a large cyst replaced the caudal pole of the pyriform lobe, all except the rostral pole of the amygdaloid complex and the whole of the remaining hippocampal gyrus. On the right the pyriform lobe (Pyr. Figs. 2–5) and amygdaloid complex (am., Figs. 1–3) were injured along their lateral margins. The origin of the stria terminalis appeared normal, but the fibers were cut just above this level. The ventral and caudal portions of the hippocampus, subiculum (Subic., Fig. 5) and praesubiculum were present, but considerably shrunken. The fornix longus and fimbria were destroyed and the alveus completely degenerated. Connections forward to the pyriform and caudalward to the remaining gyrus splenius posterior remained.

Striatum and subthalamus.[4] The head of the caudate nucleus was involved in the lesion dorsally and laterally (N.c., Figs. 1, 2) and the tail was removed on either side, so that approximately one-third of each nucleus had been destroyed. On the left only the rostral half of the putamen was present and this showed injury dorsally and laterally; on the right the whole of the medial half remained (Put., Figs. 1–3). The globus pallidus was intact on both sides and appeared essentially normal (Gl., Figs. 1–3). The entopeduncular nucleus (N. ent., Figs. 1–4) the zona incerta (Z. i., Figs. 3–5), the subthalamic nucleus (N. sub., Fig. 5), the fields of Forel (H_1 and H_2, Figs. 3–5), the substantia nigra (S. n., Fig. 28) and the red nucleus (N. r., Fig. 28) were not involved in the lesion on either side. The cells were somewhat crowded, particularly in the substantia nigra, but no intrinsic abnormalities were apparent.

Thalamus. The dorsal thalamus was involved in the lesion about equally on

[4] The terminology employed here and in the following anatomical descriptions will be that used by one of us previously (31).

the two sides, and the remaining nuclei were considerably shrunken and distorted. Of the anterior group only the nucleus antero-medialis was present (N. a. m., Fig. 2). Medial nuclear group: the nucleus centralis lateralis and the dorso-lateral and lateral portions of the nucleus medialis dorsalis had been removed. The remaining portion of the nucleus medialis dorsalis (N. m. d., Figs. 3, 4), the nucleus parataenialis (N. p-t., Fig. 2), the nucleus paracentralis (N. p-c., Fig. 3) and the nucleus submedius showed considerable degeneration, though there were still numerous myelinated fibers connecting with the midline systems, with the remaining portions of the nucleus ventralis and with the external medullary lamina. The internal medullary lamina (L. m. i., Fig. 3) was greatly reduced in size. The nucleus parafascicularis (N. p-f., Fig. 4) was relatively normal, but the centre median of Luys (c. m., Fig. 4) was indistinct. Midline group: the third ventricle was markedly dilated and the midline group of nuclei reduced in size and distorted. The periventricular system appeared relatively intact throughout. The rostral members of the group could not be identified and there were very few commissural fibers in this region. The caudal pole of the nucleus centralis medialis (N. c. m., Fig. 3), however, was better preserved and the commissural portion of the ventral nucleus showed relatively little change (N. v. c., Figs. 3, 4). Lateral group: the nucleus supragenicularis (N. s-g., Fig. 5), the nucleus posterior (N. p., Fig. 5) and the medial part of the caudal pole of the nucleus lateralis were present. These contained a few myelinated fibers, running mainly towards the external medullary lamina. Ventral group: only the medial and caudal portions were present (N. v., Figs. 3, 4). These appeared shrunken but were filled with a rather dense plexus of fibers. There were numerous connections with the external medullary lamina, the subthalamus, the periventricular system and the medial geniculate body, but none of the typical, large bundles of fibers which normally connect with the internal capsule were present. *Metathalamus.* The lateral geniculate bodies had been cut through on both sides rostro-laterally (N. g. l. d. and v., Fig. 5). The optic tracts were apparently intact. The medial geniculate bodies were not involved in the lesion. They showed a moderate, general shrinkage in size, however, particularly of the nucleus principalis (N. g. m. p., Fig. 5). *Epithalamus.* The striae medullares (St. m., Figs. 1–3) were considerably reduced in size, and the left stria was cut through just rostral to the habenular ganglion. The habenular nuclei (Hab., Figs. 3, 4), together with the commissure (Com. h., Fig. 5) and the habenulo-peduncular tracts (T. h-p., Figs. 4, 5), appeared entirely normal.

Hypothalamus. The hypothalamic (Hyp., Figs. 3, 4) and preoptic areas (A. p-o., Fig. 2) were not involved in the lesion and no gross abnormalities were apparent, other than the absence of the fornix and stria terminalis and a reduction in size of the bundle of Vicq d'Azyr (T. m-th., Figs. 4, 5).

Mesencephalon, medulla, spinal cord. The changes noted consisted of degeneration of the peduncles, moderate reduction in size of the pons and degeneration of the pyramids. There was some general shrinkage of the reticular substance.

Following is a brief account of this cat's general characteristics, with mention of the simple responses which were always evocable. Apart from brisk pupillo-constriction and closure of lids on illumination of the eyes, no visual reactions of any kind were found. Certain auditory responses were easily obtained. A light whistling noise, the sound made by sandpaper rubbing against wood or other noises of high pitch and low intensity, evoked elevation and pointing of the ears, widening of the palpebral spaces and turning of the head toward the source of the sound. Whenever this response was repeatedly elicited, it became less marked and eventually disappeared, only to return after a period free from auditory stimulation of the adequate type. The acoustic reflexes exhibited by the chronic decerebrate cats of Bazett and Penfield (9) were elicited by stimuli of a similar nature. These authors, however, report no evidence indicating orientation of the animal or of its head in respect to the source of the sound. Correlated with the anatomical integrity of a large part of the central olfactory mechanism was a definite response to certain odors. Most striking was the sniffing, licking, and moving about with mouth close to the floor when an odoriferous food (*e.g.*, fish) was placed nearby. After a hearty meal this behavior could not be evoked and it was most intense when food had been withheld for some time. There was apparently no ability to locate the source of odors, and unless food was placed directly in front of the animal it was reached only by chance. The postprandial chop- and nose-licking with dorsiflexion of the head, which is seen in normal cats, was greatly exaggerated and prolonged in this animal. Certain responses resulted from various cutaneous stimuli. When a paw was wet or soiled, it was sometimes held lifted from the floor and occasionally licking movements accompanied this posture, but rarely were they accurately directed to the foot. Gentle rubbing of any part of the body surface except the head induced vigorous licking and when the cutaneous stimulus was made stronger (*e.g.*, scratching) biting occurred. When the dorsal midline was thus stimulated, these responses of tongue, mouth, head and neck were directed forward and downward so that the cat licked and bit at the floor between its forefeet. Advantage was often taken of this reaction to speed or to extend the ingestion of food. When the cutaneous stimulus was to

one side of the midline, the head slowly turned to that side, but it was seldom that the animal licked or bit the area stimulated. When mange was present this reaction was so intensified that the animal would often bite its chest, shoulders or flanks and during the last weeks of her career, when many self-inflicted wounds provided a continuous source of irritation, slight cutaneous stimulation often evoked a generalized convulsion in which the animal tore viciously at its skin.

On the twenty-ninth day following the final cerebral ablation it was discovered by chance that insertion of a clinical thermometer into the distal vagina immediately induced loud growling, lowering of chest and head, elevation of pelvis and tail and treading movements of the hindlegs. After removal of the stimulus the cat executed vigorous squirming movements on her side and playfully rubbed her cheek and occiput against the floor. Some experience with cats which had entered into "heat" in the laboratory made it impossible to mistake the nature of this performance. It was at once apparent that she was exhibiting one phase of the typical feline oestrual behavior. Crouching and treading occurred at this time whenever a gentle mechanical stimulus, such as rubbing or tapping, was applied to the vulva or to the skin area immediately surrounding it. This specific response to genital stimulation lasted from the twenty-ninth to the fifty-eighth postoperative day and recurred for a few days during the eighth month. At all other times it could not be obtained. Vaginal smears showed the cellular picture characteristic of feline oestrus only when the behavior described above was evocable. Also it was solely at this time that she attracted males. On becoming the object of the attentions of a sexually excited male she exhibited oestrual behavior, but only in response to stimulation of her genital region. To such preliminary advances as vocalization and licking of her head she appeared entirely indifferent. Even when the male mounted and executed treading movements of the legs, she showed no actual oestrual response. Squatting flat on the floor she licked vigorously in response to incidental cutaneous stimulation. When he grasped her too violently by the nape of the neck or pulled her about, she spat, growled and lashed her tail. If, however, he pressed against her external genital region she immediately assumed the full oestrual

crouch and treaded with tail elevated and laterally deflected. Intromission, signalled by typical vocalization on the part of the female and confirmed by finding spermatozoa in vaginal smears, occurred three times. On each of these occasions, after the male had dismounted, she turned onto her side, rolled and playfully rubbed her head with her forepaws. Such is the "after-reaction" shown by normal females after coitus. When in dioestrus, 103 showed no trace of this behavior in response to genital stimulation.

Specific deficiency phenomena were of course prominent in this animal and a few have already been mentioned. A recent paper (3) has described and analyzed the postural defects of this and other decorticate cats. Locomotion was good, but not quite normal. The occurrence of walking could sometimes be correlated with either hunger or a distended bladder or rectum. In spite of abnormal attitudes of the legs during standing, sitting and crouching the animal assumed, during defecation and micturition, the posture characteristic of normal cats. Although the chest and forelegs were licked spontaneously, there was failure to keep the rest of the body surface clean. The coat became matted and filthy unless it was brushed and at times baths had to be resorted to. The cat slept as do normal cats, but when fully asleep it was necessary to shake or handle her or to apply a nociceptive stimulus in order to awaken her. This was also observed by Kleitman and Camille (23) in their study of sleep in decorticate dogs. Often on being awakened and at other times this cat went through typical stretching movements, occasionally accompanied by yawning. Less frequently, after stretching, she would extend her claws and forelegs and scratch the floor in the manner of a cat "sharpening" its claws on a post or tree.

(2) *Cat 313*

This was a female which at the time she entered the laboratory was exceedingly wild. During the five months which elapsed before her first operation she was always very timid, ran off whenever approached and made frantic attempts to escape when caught. It proved impossible to tame her, although she spontaneously became tractable for a short time following the birth of kittens. These characteristics remained unaltered after the removal, on July 27,

1932, of essentially all neocortex of the left hemisphere together with the dorsal half of the hippocampus and the most lateral part of the pyriform lobe. On October 15, 1932, a similar operation was performed on the right side. Recovery was rapid and within a week she presented a picture almost identical with that observed in the case of cat 103 throughout the first twenty months of survival. Cat 313 remained in excellent health for six weeks and then suddenly succumbed to an acute respiratory infection (pneumonia with pleurisy). The brain (Fig. 22) was immediately removed and preserved in 95% alcohol for microscopic examination. It was sectioned serially at 30 μ. Every fifth section was stained with thionin and mounted.

Neopallium. A small fragment of the gyrus proreus in front of the septum remained on either side.

Rhinencephalon. The olfactory stalks had been transected just rostral to the tuberculum olfactorium. The latter (Tub. ol., Fig. 6) was injured along its lateral border on the left, the medial olfactory areas and septal nuclei (N. p-ol. m. and l., Fig. 6) being otherwise essentially intact. The pyriform lobe and amygdaloid complex (Pyr. and am., Figs. 6–8) were involved in the lesion along their lateral margins on the left, and showed moderate gliosis. On the right only the medial third of the pyriform lobe remained and the amygdaloid complex was largely destroyed. The stria terminalis (St. t., Figs. 6–11) was present on the left, but destroyed on the right. The ventral two-thirds of the hippocampus (Hip., Figs. 9–11), with the subiculum (Subic.), presubiculum and entorhinal cortex (Ent., Figs. 10, 11), were present on the left and attached to the pyriform lobe in front. The dorsal third, with the fornix, was destroyed. On the right only a ventral fragment remained (Hip., Figs. 9, 10).

Striatum and subthalamus. On the left the lesion involved the dorso-lateral part of the head of the caudate (N. c., Figs. 6, 7) and the lateral margin of the putamen (Put., Figs. 6–8), but the tail of the caudate and the globus pallidus (Gl., Figs. 6–8) were spared. On the right the lesion was more extensive, destroying the tail of the caudate and almost the entire putamen, and injuring the lateral margin of the globus pallidus. The nucleus entopeduncularis (N. ent., Figs. 6–8), the zona incerta (Z. i., Figs. 7–10), the nucleus subthalamicus (N. sub., Fig. 9), the fields of Forel (H_1 and H_2, Figs. 9, 10) and the substantia nigra (S. n., Fig. 11) were intact, but the cells appeared crowded. This abnormality was least evident in the nucleus entopeduncularis and the fields of Forel. The red nucleus (N. r., Fig. 11) appeared normal.

Thalamus. Excepting slight injury to the dorsolateral border of the lateral nucleus on the right there was no evidence of operative trauma to the thalamus. The extensive changes found were symmetrical and were apparently due to secondary degeneration. Anterior nuclear group: the medial part of the nucleus

antero-medialis (N. a. m., Fig. 7) appeared essentially normal, but the remainder of the group had degenerated except for an occasional cell. Medial nuclear group: the nucleus parataenialis (N. p-t., Figs. 7, 8) was well preserved, as was the dorsal half of the nucleus medialis dorsalis (N. m. d., Figs. 8, 9) adjoining it. The ventral half of the latter nucleus contained only a few surviving ganglion cells. The nucleus submedius could not be identified though there were numerous apparently normal cells in that region. The nuclei tractus habenularis lateralis and parafascicularis (N. p-f., Fig. 9) appeared normal. The nucleus paracentralis (N. p-c., Figs. 7, 8) showed a moderate loss of ganglion cells, but the nucleus centralis lateralis (N. c. l., Fig. 7) was entirely degenerated. Midline nuclear group: this was the best preserved portion of the thalamus. There was a general shrinkage in size of the whole group with crowding of the cells which made it difficult to determine the boundaries of the different nuclei. The actual loss of ganglion cells was very slight, occurring mainly in the ventral half of the nucleus centralis medialis and in the rostral half of the nucleus ventralis pars commissuralis (N. c. m. and N. v. c., Fig. 8). Lateral nuclear group: the nucleus lateralis (N. l., Figs. 7, 8) contained only fibers and glia besides a few pale, shadowy ganglion cells in the pars anterior. The pulvinar was likewise entirely degenerated, but there were a few normal appearing cells in the nucleus suprageniculatus and a greater number in the nucleus posterior (N. s-g. and N. p., Figs. 9, 10). The cells of the whole of the nucleus reticularis thalami (N. ret., Figs. 7–9) were essentially normal, but considerably crowded together and there was extreme gliosis throughout this region. Ventral nuclear group: the anterior and lateral portions of the nucleus ventralis (N. v., Figs. 7–9) were almost completely degenerated, with only occasional ganglion cells remaining. The pars commissuralis, pars medialis and the region of the caudal pole were better preserved, showing only a moderate loss of cells. The centre mediàn (c. m., Fig. 9) had also suffered almost complete loss of cells, its position being clearly defined by the fiber arrangement. *Metathalamus:* the lateral geniculate bodies had been injured dorso-laterally and showed rather marked gliosis. The remaining tissue of the dorsal nuclei (N. g. l. d., Figs. 9–11) preserved its typical laminar structure, though somewhat more than half of the cells were merely pale shadows. The ventral nuclei (N. g. l. v., Figs. 9–11) and the optic tracts (Tr. op.) appeared normal. Both medial geniculate bodies were slightly reduced in size, the majority of the ganglion cells were very pale, and there was moderate gliosis, particularly in the rostral halves of the nucleus principalis (N. g. m. p., Figs. 10, 11). The pars magnocellularis (N. g. m. m.) was apparently normal.

Preoptic and Hypothalamic Areas. There was moderate gliosis in the region of the degenerated fornix and a general shrinkage in size of the whole region. Otherwise these areas appeared normal (Hyp., Figs. 7, 8).

Mesencephalon and Medulla. The peduncles (P. p., Figs. 9–11) and pyramids were degenerated and showed marked gliosis. The pons was smaller than normal and showed slight gliosis, but no nuclear changes. The substantia reticularis appeared slightly shrunken in size, but no other abnormalities were noted.

Because of the secondary degeneration present in the thalamus the main difference between this brain and the brain of cat 103 was that in the former the olfactory stalks had been severed. This condition accounts for the only definite difference observed in the behavior of the two animals. At no time did cat 313 show any response to olfactory stimuli. When mouth and tongue were placed in contact with a sapid food substance, she ate of her own accord, and so long as the food was kept within immediate reach of the mouth, she continued to eat until a large meal had been consumed. After food had been withheld for some time, and in the absence of any specific olfactory stimulus, this animal invariably began to lick the floor and to move about restlessly. The longer the food was withheld, the more intense was this activity; it never occurred during the hours following a meal. In short, a state which may be called hunger induced in this anosmic animal behavior very similar to that shown by cat 103 under the same circumstances. But the sniffing, so characteristic of 103, did not occur. In other respects the general behavior of the two animals was the same.

(3) *Cat 244*

This animal was subjected to a somewhat more extensive removal of cerebral tissue than were cats 103 and 313. It was a rather small, mature female. During a pre-operative observation period of three weeks she showed herself to be very friendly, active and alert. The operation on the right side of her brain was carried out on November 3, 1931. The entire neocortex, the olfactory bulb and stalk, the lateral part of the pyriform lobe, most of the hippocampus, the lateral portions of the striatum and all the thalamus except the midline nuclei were removed (see Fig. 25). This ablation produced deficiencies no greater in number or extent than those observed in cats 103 and 313 after less extensive unilateral removals of forebrain tissue.

Following this first cerebral ablation cat 244 exhibited a most striking rage reaction in response to light mechanical stimulation of her *right* side. With the exception of the periods noted below this was evocable throughout the eight months which elapsed between the two intracranial operations. Nothing of the sort was ever seen during

the observation period of three weeks which preceded the first ablation. Gently rubbing or lightly pinching the right flank, hip, shoulder, arm, leg or ear evoked spitting, growling, quick turning to the right and powerful, accurately executed, striking movements of the right foreleg. When the stimulus was applied while the animal was being restrained or confined, it induced a savage attack in which angry vocalization, bilaterally equal pilo-erection and pupillo-dilatation, retraction of ears, clawing with all four feet and biting were prominent features. Unless definitely "cornered" the cat sought sooner or later to escape and would, if possible, run off spitting, growling and lashing her tail. Although this response was not at all dependent upon coincidental visual or auditory stimuli, perception of any moving object directed toward the right side of the body usually caused spitting and striking. When the rage reaction was repeatedly evoked, its ferocity and vigor increased. Its threshold was quite low over the entire right half of the animal, but was lowest at apical points, the ear and the two feet. Stimuli adequate to elicit the reaction from points on the right side failed to do so when applied to symmetrical points on the left side. When the left side of her body, head or neck was vigorously stroked or rubbed, this cat displayed indifference or mild pleasure. The tremendous contrast in the effect of stimulating the two sides of the body was readily demonstrated by slowly stroking the animal transversely from left to right. The instant the stimulus crossed the ventral or dorsal midline the rage reaction abruptly appeared. It was possible, however, to induce the full response by applying a sufficiently strong stimulus to the left side. Here the effective stimulus was definitely nociceptive, whereas on the right side a light touch, just sufficient to displace the hair, was entirely adequate. In contrast to the excessive response induced by an external agent (the observer, another cat, etc.) was the marked tendency of the animal to rub or press with apparent enjoyment the right side of its head or body against solid objects such as a wall, a table leg or an observer's ankle.

The reaction did not persist after the second intracranial operation. It was subject to certain minor variations. For instance, its threshold was raised during an infection of the upper respiratory tract. Whenever the animal was placed in strange surroundings or frightened by barking dogs, this rage response could not be evoked even by strong

stimulation. During two periods of oestrus it was impossible to elicit it, and at these times any stimulus which was not nociceptive provoked only oestrual behavior. At the second oestrus the animal was mated and became pregnant. On May 25, 1932, she gave birth to four kittens. During the latter part of pregnancy the reaction could be evoked only in mild form and by strong pinching of the right side. It returned within a few days following parturition, but was not provoked by the nursing of the kittens on either side.

On July 14, 1932, in an operation on the left side of the brain, all neocortex, much of the rhinencephalon, practically the whole striatum and a large portion of the thalamus were removed. After an uneventful recovery the animal remained in good health until sacrificed on June 16, 1933. The brain (Fig. 23) was removed at autopsy, fixed in alcohol, imbedded in celloidin and cut serially at 30μ. Every tenth section was stained with thionin and mounted.

Neopallium. Entirely removed.

Rhinencephalon. The olfactory stalks were transected near the base of the brain. The left tuberculum olfactorium was injured laterally, the right was intact (Tub. ol., Fig. 12). The septal nuclei were destroyed and the diagonal band of Broca (Diag. B., Fig. 12) appeared shrunken and showed considerable gliosis, with moderate loss of ganglion cells, particularly on the left. The nucleus accumbens could not be defined and the bed nuclei of the anterior commissure and of the stria terminalis (N. st. t., Fig. 12) were not clear. Apparently the caudal portions were still present, but the cells were crowded and there was considerable gliosis. On the left the lateral half of the pyriform lobe (Pyr., Figs. 13, 14) was destroyed and only the ventro-medial portion of the amygdaloid complex (am., Fig. 13) remained. On the right the lesion passed through the lateral margins of both these structures. The anterior commissure (C. a., Fig. 12) was entirely degenerated and the stria terminalis destroyed. The ventral end of the hippocampus, with the attached subiculum and praesubiculum (Hip., subic., pre-sub., Fig. 15) was present on both sides and connected with the remaining portions of the pyriform lobes. The lesion passed through the entorhinal cortex (Ent., Fig. 15).

Striatum and Subthalamus. The caudate nucleus had been removed on both sides except a few cells of the caudo-ventral part of the head. The putamen was entirely destroyed on the left, but on the right a fragment of its basal portion remained and showed marked gliosis (Put., Figs. 12, 13). A few median cells of the globus pallidus remained on the left. On the right the globus pallidus (Gl., Figs. 13, 14) appeared essentially intact, though there was gliosis and some crowding of the cells. The entopeduncular nucleus (N. ent., Figs. 13, 14) was

injured on the left and showed crowding of the cells on both sides. The zona incerta (Z. i., Fig. 14) showed some gliosis rostro-laterally, but more caudally appeared intact and the fields of Forel also appeared normal. The cells of the nucleus subthalamicus and of the substantia nigra (S. n., Fig. 15) were markedly crowded together. There was slight gliosis of the red nucleus (N. r., Fig. 15) and apparently some reduction in size; the cells appeared normal.

Thalamus. The dorsal thalamus was largely destroyed. The anterior nuclear group had been entirely removed and the medial nuclear group was destroyed or replaced by glia in front of the habenulo-peduncular tracts. The nucleus parafascicularis and the nuclei of the habenulo-peduncular tracts were present, but showed gliosis. The midline nuclear group consisted of irregularly arranged cells, the whole being so distorted that none of the nuclei could be delimited (N. c. m. and N. v. c., Fig. 14). The lateral nuclear group had been destroyed in front of the level of the lateral geniculates. The lesion was slightly more extensive on the left. At the caudal pole a few ganglion cells remained just medial to the geniculate bodies. These probably represented the remains of the nucleus posterior. The rest of this region showed extreme gliosis. The pretectal area (A. p-t., Fig. 15) was involved in the lesion on both sides, more on the left than the right. The nucleus reticularis thalami was destroyed except the caudal pole of the ventral portion on the right. Ventral nuclear group: the anterior two-thirds had been destroyed and there was extreme gliosis and loss of ganglion cells in the remaining lateral portions, more extensive on the left than on the right. The pars commissuralis (N. v. c. Fig. 14) was present, but also showed gliosis and a considerable loss of ganglionic elements. *Metathalamus:* The external two-thirds of the lateral geniculate body was destroyed on the right, somewhat more than this on the left (N. g. l. d. and v., Fig. 15). The remaining fragments showed extreme gliosis and a large proportion of the ganglion cells were mere shadows. The optic tracts (Tr. op.) appeared normal. The rostral pole of the left medial geniculate body had been injured by a stab wound which passed just medial to the lateral geniculate. Both medial geniculates were considerably shrunken and showed gliosis, mainly in the nucleus principalis (N. g. m. p., Fig. 15). There was some loss of the ganglionic elements. *Epithalamus:* The stria medullaris had been cut and was replaced by glia (St. m., Figs. 12–14). The habenular ganglia were present, but shrunken in size and the cells crowded. There was moderate gliosis, but no change in the ganglion cells. The habenulo-peduncular tracts appeared normal (T. h-p., Fig. 15).

Hypothalamus. The preoptic area and the hypothalamus were not directly involved in the lesion (A. p-o. and Hyp., Figs. 13, 14). They showed considerable general shrinkage in size and, in the lateral hypothalamic areas, moderate gliosis.

Mesencephalon, medulla oblongata. The peduncles (P. p., Fig. 15) and pyramids were degenerated and gliotic. There was shrinkage in size and gliosis of the pons, but no cellular changes were apparent. The reticular substance showed slight gliosis in the region of the midbrain and was reduced in size throughout, but no chromatolysis was apparent.

The general behavior of this surviving "decorticate" preparation differed only in certain respects from that of cat 103, already described. Like cat 313 it exhibited no olfactory responses and it ate less readily of its own accord than either 103 or 313. During the greater part of its survival it was necessary sometimes to initiate and often to extend the taking of food by rubbing its back, a procedure that in each of these animals invariably produced vigorous licking and biting. The cat indulged in more coat-licking than the other decorticate animals and this activity was directed to the left foreleg and shoulder and the left side of the chest. As a result the hair over this region was clean and smooth; elsewhere it tended to become matted and filthy as in the other cats. A singular and very striking item of behavior appeared during the latter six months of the survival period. At times when the animal was allowed the freedom of a large laboratory room it was noticed that she followed one about. On several occasions she followed different observers out into a corridor, along it for a distance of from ten to twenty yards and back again into the room. At other times it was impossible to obtain this response and we were unable to determine the conditions favoring it. That the adequate stimulus was auditory seems certain. When following was evocable her responses to sounds were particularly brisk and she would often turn and walk or even run toward the source of a light whistle or of a scraping noise. A similar phenomenon was observed by Dusser de Barenne (12) in his cat II.

(4) *Cat 228*

In the case of this animal (a middle-aged female) the surgical objective was the production of a hypothalamic preparation. However, as indicated below, the ablation was not quite so great as was intended. Nevertheless, there was a much more extensive removal of subcortical structures than was effected in any one of the other preparations. The removal of cerebral tissue from the left side was carried out on September 8, 1931. The only result of this procedure, which differed from that obtained in many cases of unilateral decortication with or without involvement of the striatum, was a widely dilated and fixed left pupil which remained permanently unresponsive to illumination of either retina. Before operation this animal displayed certain

traits: an unusual amount of exploratory activity in any strange environment; friendliness, and apparent enjoyment on being petted; gentleness when handled in any reasonable fashion. These characteristics were in no wise altered by the first cerebral ablation. The second operation (on the right side of the brain) was done on December 23, 1931. For more than a year the animal remained in good health. Finally, toward the end of the thirteenth month, and shortly after being subjected to several bouts of alcoholic intoxication, she developed symptoms of destruction of the left labyrinth. These were accompanied by signs of infection of the upper respiratory passages and on February 3, 1933, the animal was killed. Autopsy revealed a chronic infection of the frontal sinuses and of both tympanic bullae. On both sides, but more extensively on the left, the inner ear had become involved. The cranial cavity had not been invaded by these pathological processes.

The brain (Fig. 24) was fixed in formalin, imbedded in celloidin and cut serially at 40μ. Every tenth section was stained by the Weigert-Pal method and alternate fifth sections by the Weil method.

Neopallium. Entirely removed.

Rhinencephalon. The olfactory stalks together with almost the whole of the tuberculum olfactorium had been removed. The caudo-medial portion of the latter remained on the left side (Tub. ol., Fig. 16). Of the septal nuclei, the caudo-ventral half remained on the left, but only a small fragment on the right (N. p-ol. m. and l., Fig. 16). The lesion passed through the most lateral part of the diagonal band of Broca on the left, the main body of the band appearing normal (Diag. B., Fig. 16). On the right the band was cut in half and the remaining medial portion contained no large fibers or cells. The lateral halves of the nucleus accumbens (N. ac., Fig. 16) and of the bed nuclei of the anterior commissure and of the stria terminalis (N. st. t., Fig. 17) were destroyed on the left. On the right these structures had been entirely removed. A small piece of the pyriform lobe (Pyr., Figs. 17, 18) was present on the left, but the amygdala was destroyed. On the right both the pyriform lobe and the amygdala had been removed. The stria terminalis was destroyed bilaterally and the anterior commissure was entirely degenerated. A fragment of the ventral pole of the hippocampus was present on both sides, but it appeared doubtful whether this had been functional during life (Hip., Fig. 18).

Striatum and Subthalamus. On both sides the nucleus caudatus, putamen and globus pallidus had been entirely removed. On the left the caudal pole of the entopeduncular nucleus was present (N. ent., Fig. 18), but on the right it could not be clearly defined. The zona incerta (Z. i., Figs. 18, 19) was involved rostro-

laterally on both sides. The nucleus subthalamicus was bilaterally present, but was small and rather distorted (N. sub., Fig. 19). The field H_1 of Forel appeared essentially normal (H_1, Fig. 19), but there were few fibers in the field H_2 (H_2, Fig. 19). The substantia nigra (S. n., Figs. 20, 29) was small and distorted, the cells being very crowded together. The red nucleus (N. r., Figs. 20, 29) was smaller than normal, and there was a reduction in the fibers, especially laterally and rostrally.

Thalamus. The anterior nuclear group had been removed except the medial portion of the nucleus antero-medialis (N. a. m., Fig. 18). Medial nuclear group: the nucleus para-taenialis (N. p-t., Fig. 18) and the nucleus medialis dorsalis (N. m. d., Fig. 19) were involved laterally on both sides except at the caudal poles. They appeared shrunken and there was a marked loss of fibers. The nucleus centralis lateralis had been removed and the nucleus paracentralis was shrunken and contained relatively few fibers (N. p-c., Fig. 18). The nucleus parafascicularis (N. p-f., Fig. 19) was involved laterally, but the fiber content was essentially normal. Midline nuclear group: this group of nuclei was not directly involved in the lesion, but nevertheless appeared considerably smaller than normal. Of the individual nuclei only the inter-parataenialis, the inter-antero-medialis, the centralis medialis (N. c. m., Fig. 18) and the pars commissuralis of the ventral nucleus could be identified. Throughout there was a great reduction in the number of large commissural fibers, which was more marked rostrally than caudally. The periventricular system was reduced in size, though numerous fine fibers connecting with the hypothalamus were still present. The connections to the internal medullary lamina were relatively few. Lateral nuclear group: this had been almost entirely removed bilaterally, only the medial third of the area pretectalis still remaining (A. p-t., Fig. 20). Ventral nuclear group: the lateral portions had been removed and the lateral borders of the pars medialis were involved in the lesion on both sides. The pars commissuralis appeared fairly well preserved. *Metathalamus*: the lateral geniculate bodies on both sides, including the dorsal and ventral nuclei, had been removed. The optic tracts were cut through, the right a few millimeters from the chiasma, the left about half way between the chiasma and the lateral geniculate. The optic nerves were not involved. Nevertheless, there were only a few, large, myelinated fibers remaining, the greater part being completely degenerated. Both medial geniculate bodies were destroyed except the most caudo-medial poles (N. g. m., Fig. 20), the point of entry of the brachium of the inferior colliculus. The brachium (Br. c. i., Fig. 20), on the other hand, appeared normal. *Epithalamus:* the striae medullares were greatly reduced in size, but the remaining fibers appeared normal (St. m., Figs. 17–19). The habenular ganglia and the habenulo-peduncular tracts showed no definite pathological changes (Hab. and T. h-p., Fig. 19).

Hypothalamus and pre-optic areas. On the left these areas were not directly involved in the lesion (A. p-o. and Hyp., Figs. 17, 18). On the right the rostral pole of the medial pre-optic area was cut through and this, together with almost all of the lateral pre-optic area, was removed. The whole hypothalamus was considerably reduced in size and the medial forebrain bundle was absent.

Mesencephalon. The brachia of the superior colliculi were cut through. There was fiber degeneration in the superior colliculus (Col. s., Fig. 20) and the lamination was indistinct, especially rostrally. The inferior colliculus appeared normal. The cerebral peduncles were entirely degenerated (P. p., Fig. 20). There was general shrinkage in size of the reticular substance.

Medulla. The pons showed marked loss of fibers, the pyramids were completely degenerated, and there was considerable shrinkage in size of the reticular substance.

In view of the extent of the ablation it is not surprising that this cat proved to be the most abnormal of the four. Her postural deficiencies were outstanding. In common with 103, 313 and 244 she tended to assume peculiar attitudes of the legs while standing, sitting or crouching, but she fell into these more readily and maintained them for longer periods of time. In a recent communication (3) it has been indicated that this peculiarity of decorticate cats is due to a deficiency of the placing and hopping reactions. Although these specific responses were not more deficient in 228 than in the other decorticate cats the abnormal leg attitudes were doubtless made more prominent by her tendency to remain standing, sitting or crouching for longer periods of time. Certainly she showed less spontaneous activity. Her walk was more abnormal. Moving slowly and awkwardly, with head lowered and pelvis elevated, with each hind foot dragging slightly at the beginning of a somewhat circumducted step and with a wide base for the hindlegs she progressed ponderously and deliberately in a distinctly reptilian fashion.

In the matter of taking food No. 228 was the most deficient of the four cats. Occasionally she licked a few times when lips and tongue were brought into contact with food, but she never really ate of her own accord. Throughout her survival it was necessary to feed her either by putting food into her mouth or, more conveniently, by rubbing some part of the body surface while a bowl of food was held below her mouth. Although she frequently licked the floor, her tongue was never applied to her own body and her coat remained matted and disorderly unless it was brushed daily. On one occasion she was observed to execute, while standing, alternate movements of the forelegs with claws unsheathed. This performance was very like the type of activity which is popularly termed "claw sharpening" and which normal cats usually practice in an upright posture with forelegs against a tree or post. As would be expected from the ana-

tomical findings she showed no trace of any visual response; both pupils were fixed in a state of extreme dilatation and blinking was induced only by stimulation of the lids or adjacent structures. She failed to show the very specific auditory responses which were evocable in the other cats, and it is possible that their absence was due to the removal of the medial geniculate bodies. Since, however, auditory responses have been elicited in cats after an intercollicular transection (9, 14), one might expect to find some response to sounds in this less reduced surviving preparation. As a matter of fact, one was found and its character was most peculiar. When a loud blast was blown on a bugle or a police whistle (but never when less strident sounds were made) the animal responded by twitching the skin of her back and by a very pronounced erection of the hair of back and tail. There was also a widening of the palpebral fissures, but no other reactions were observed. This response to an intense auditory stimulus was first observed on the twelfth postoperative day and it was repeatedly obtained thereafter. Such were the specific peculiarities of this animal. In other respects she closely resembled the three cats already described.

II. DESCRIPTION AND DISCUSSION OF CERTAIN REACTION PATTERNS

In order to facilitate comparisons between the four animals under consideration the main anatomical features have been diagrammatically summarized in Figure 25.

(1) *Rage Reactions*

From the descriptions of decorticate animals given by earlier writers (12, 16, 33) it could be inferred that the nervous mechanisms which actually elaborate the expressions of anger characteristic of the normal dog or cat are located subcortically and become somewhat hyperexcitable after cortical ablation. The suggestion that removal of cerebral cortex renders an animal excessively prone to display anger led Cannon and Britton (10) to use the decorticate cat for a study of one aspect of the bodily changes which constitute emotional behavior of the rage type, namely, sympatho-adrenal activity. In acute experiments on cats they found that after disconnecting the cortex from the brain stem there ensued upon removal of the anesthetic

(ether) "a group of remarkable activities such as are usually associated with emotional excitement—a sort of sham rage." In their experiments the animals were secured on an animal board and under such conditions the phenomena constituting sham rage usually developed in the absence of any special provocation. They usually occurred in fits; during the intervening periods of comparative quiet a paroxysm could be brought on by any mild disturbance of the animal. The activity included struggling, attended by movements of the head from side to side and arching of the trunk with thrusting and pulling of the limbs, clawing movements of the forelimbs with protrusion of the claws, waving and lashing of the tail and a snarling or hissing expression. This activity in skeletal muscle was accompanied by signs of vigorous sympathetic discharge: erection of hair, sweating, retraction of nictitating membranes, pupillc-dilatation, exophthalmos, rises in arterial pressure and evidence of augmented medulliadrenal, secretion (acceleration of the denervated heart). In intensity and pattern this behavior was unmistakably the counterpart of the activity which characterizes intense fury in the normal animal. Indeed an unruly normal cat, when restrained in a similar manner, will display activities which are identical with those of the sham rage of the acute decorticate preparation.[5]

In 1928 Bard (1), employing the method of cerebral ablation, was able to show that the central mechanism essential for the occurrence of sham rage in the cat lies within the ventro-caudal portion of the diencephalon (*i.e.*, in the caudal hypothalamus). At the same time he suggested that this delimitation threw some light upon the significance of the results of those investigators such as Karplus and Kreidl, who had obtained sympathetic discharges by applying stimulating currents to the hypothalamus. The view was advanced that the hypo-

[5] The word rage, when used without qualification, implies both a way of acting and a mode of feeling. Therefore, the expression "sham rage" was adopted by Cannon and by Bard (a) to indicate that in the case of the decorticate preparation one is dealing only with an *expression* of anger and (b) to suggest the probability that cortical ablation profoundly modifies the subjective aspect of rage. The adjective "sham" unfortunately suggests something false or counterfeit, but the sham rage displayed by a decorticate cat very closely resembles the behavior of the infuriated normal animal. Doubtless it would have been more accurate to have used the expression "quasi-rage."

thalamic representation of the sympathetic consists of mechanisms which are responsible for the activation of that division of the automatic system under conditions of physiological stress, especially during emotional excitement and exposure to cold. The recent work of Ranson and his collaborators, in which this region of the brain was systematically explored by stimulating electrodes, has yielded further evidence (21, 30) that the hypothalamus is responsible for the elaboration and execution of the complex reaction pattern which is characteristic of rage.

The excessiveness and easy elicitation of the sham rage suggest that it is a release phenomenon in the sense of Hughlings Jackson. Thus its occurrence might be due to the freeing of a hypothalamic mechanism from cortical restraint. On the other hand, there is, in any acute experiment involving ablation of cerebral tissue, the possibility that some sort of "irritation" may be a causative factor in producing a positive result. One experimental fact, however, indicates that direct irritation from injury is probably not so significant a factor in the genesis of sham rage as may at first sight appear. In the first series of acute experiments (1) and in a larger number carried out subsequently for various purposes, it was found that the sham rage developed in the same form and with the same intensity after simple decortication with minimal injury to brain stem as after transection at any subcortical level—down to the caudal diencephalon. Yet it would be hazardous to claim that irritation played no rôle in the production of the activity in these acute experiments. Therefore we have turned with special interest to a study of the rage reactions of healthy long-surviving decorticate cats. In them any tendency to react excessively must be attributed to some sort of release.

On the seventh day following the final cerebral ablation (done under sodium barbital with emergence on the third day) cat 103 growled and lashed her tail while being brushed. At the same time it was observed that pinching her tail induced louder growling, spitting and turning the head to the left. On the eleventh day and from that time forth (except when the animal was ill) this stimulus evoked a stereotyped reaction consisting of: lowering the head and forepart of the body into a crouch, raising the back, drawing back the ears, loud angry growling, frequent hissing, biting, vigorous alternate striking move-

ments of forelegs with unsheathed claws, turning (almost always to the left), erection of the hair of tail and back, pupillo-dilatation, retraction of nictitating membranes and widening of the palpebral fissures. On several occasions the cardiac acceleration which always accompanies such activity was followed; the resting rates taken just before inducing the reaction varied from 70 to 100 a minute and the counts made immediately after cessation of the stimulus exceeded 200 and once reached 250.

This behavior lacked no item of the activity exhibited by a normal cat when enraged and aggressive. It varied from the display of rage seen in normal cats mainly in being undirected and stationary. The striking with unsheathed claws, the biting and the turning certainly indicated attack. At the beginning of the response the biting was directed to the region just beneath the jaws and any object placed there was viciously chewed. Then as the head was turned she often bit her flank, hindleg or hip. Meanwhile the forelegs described striking movements downward and forward and these were not at all random or incoördinate, but quite like those employed by a normal cat in attacking another animal. However, pinching the tip of the tail could be done with impunity, for neither claws nor teeth ever reached the point of stimulation. When the same reaction was induced by pinching a hindfoot or the loose skin of the flank, the turning was always toward the side stimulated, but even then the hand doing the pinching was usually safe, so poorly was the attack directed. It is significant that the animal never made any attempt to escape or move away so long as the stimulus was being applied. Sometimes immediately after its cessation the animal would walk a few steps growling, spitting and lashing its tail. These three acts were the only parts of the activity in skeletal muscle that outlasted the stimulus. "After discharge" was minimal. It was invariably safe immediately upon stopping the stimulus to place one's finger against the cat's mouth. The only result of this was to induce the licking which usually ensued when anything was placed in contact with the lips, although a moment before, during the nociceptive stimulation, the animal had been viciously biting an object held in that position.

The ease with which the rage reaction could be induced in cat 103 varied from time to time. When digestive disturbances had brought

about a weakened condition, a strongly nociceptive stimulus was required to evoke even a growl, and toward the end of her decorticate career, when large skin areas were infected and a toxic state was doubtless present, the response could not be obtained. But over long periods of time during which the animal enjoyed excellent health there were variations in threshold and it proved impossible to correlate these with any definite condition or circumstance. At times merely rolling the tip of the tail gently between thumb and forefinger sufficed to evoke a violent reaction. At other times a strong pinch was required. Occasionally the animal exhibited the full rage reaction on being brushed or merely lifted, but for the greater part of its survival such manipulations failed to induce any sign of anger. On several occasions 103 was tied on her back to an animal board in precisely the same manner as were the cats of the earlier series of experiments (1, 10). The reaction induced by this restraint was in every detail precisely the same as that described as sham rage. There was the same violent struggling with lashing of tail, clawing, snarling and signs of greater sympathetic activity than accompanied the reaction to pinching. Heart rates of 300 a minute were recorded and profuse sweating from the toe pads of all four feet occurred. In order the better to appraise this behavior a large number of normal cats were subjected to the same restraint. The responses shown by them differed in no detail from the sham rage of decorticate cats in the acute or chronic condition.

It has already been stated that cat 313 closely resembled 103 clinically as well as neurologically. Up to the tenth postoperative day rough handling or pinching failed to induce any sign of anger. But at the end of the second week and from that time to her sudden exitus four weeks later, light pinching of the tail or grasping the loose skin of back or neck and, sometimes, mere handling produced in an even more violent form the same stereotyped rage reaction which was evocable in 103. The reaction was more violent and more easily provoked than in any of the other surviving decorticate animals. This fact may possibly be related to the extraordinary wildness and intractability that characterized this animal before the first and second cerebral ablations. Yet the difference between the rage reactions of 103 and those of 313 in the decorticate state was trivial

when compared to the very great contrast in disposition exhibited by the two animals throughout long preoperative observation periods. It appears that individual traits characterizing any one animal are not retained after ablations of the extent practiced in this group of experiments. It is of interest to contrast this finding with the observations of Rioch and Brenner (32) on cats in which only the neopallium had been removed.

The same rage reaction was evocable in cat 244 throughout the eleven months of survival, but it always required strong pinching of some part of the body to elicit it. When the animal was tied on its back it responded by a display of typical sham rage, but this usually subsided after a few moments and despite continued restraint seldom recurred. During the last two months of her survival she shared a room with a number of normal cats. It was frequently observed that the more quarrelsome of these made a practice of striking at 244 whenever she came within range. Their blows usually landed on her face or on the sides or top of her head. We were very much surprised to observe that 244 responded by holding her ground, raising the forepart of her body and striking out with one or both forefeet. After such an attack she was sometimes observed to keep one forefoot raised with claws protruded apparently ready to strike again as soon as the combat was renewed. The striking was accompanied by retraction of ears, growling, spitting, erection of hair and the ocular signs of sympathetic discharge. Her blows were, of course, not directed, and they were easily avoided by her more resourceful opponent, but when the latter pressed the attack, she invariably struck harder and more frequently. It was discovered that gently tapping her on the nose or face evoked this same response and its quality made it advisable that the observer wear gloves. She never ran away or retreated during one of these bouts. It is quite possible that the other surviving decorticate cats would have shown the same behavior had they been exposed to the attentions of pugilistic companions, but for the sake of safety each of the three was kept by itself. Since they had died or been sacrificed before this behavior was noticed in 244 the point was, unfortunately, not tested.

Because of the extent of the cerebral ablation performed in cat 228 her capacity for displaying anger was studied with considerable in-

terest. The first signs of emotional behavior were on the sixth and seventh postoperative days. It was found that pinching her tail caused loud growling, turning to the right, a definite pilomotor response, retraction of nictitating membranes and widening of palpebral spaces. There was no hissing, biting or striking. On the twelfth day the same stimulus produced spitting as well as growling, more pronounced turning, weak striking and maximal erection of hair of back and tail. Up to this time rough handling or brushing had failed to evoke any sign of anger. During the third week, however, brushing the back or flanks invariably produced the typical rage reaction. During the fourth and fifth weeks of survival this response was at its height—merely lifting her from the floor caused loud growling, spitting, clawing and the usual signs of sympathetic activity. The slightest pinching of the tip of the tail sufficed to evoke a violent reaction of the same type that was exhibited by 103. From the sixth to the tenth week a gradual diminution in the intensity and a rise in the threshold of the reaction were observed. By degrees brushing and handling became inadequate stimuli and the full rage reaction was induced only by a severe pinch or by the insertion of a thermometer into rectum or vagina. This refractory condition continued throughout the remainder of the cat's long survival. The development and gradual increase in the threshold of this response were not related to any change in the general condition of the animal; its health as judged by activity, general responses and body weight remained uniformly good until the terminal illness.

The extraordinary rage reaction which was exhibited by cat 244 during the interval between the first and second cerebral ablations has been described (p. 84). It deserves special comment, since precisely the same condition developed in six other cats after extensive unilateral cerebral removals. In each case the excessive response to very mild mechanical stimulation of the *ipsilateral* side of the body developed almost immediately upon emergence from the anesthesia and has been evocable throughout survival periods of from two months to five years. All but two of these cats were gentle and friendly during long preoperative observation periods and at that time showed no signs of anger on being handled or subjected to vigorous rubbing of their bodies. The conditions governing the elicitation of this rage behavior were such as to make it almost impossible to relate it to any known clinical or experimental syndrome. Considering the trifling intensities of the mechanical stimuli which sufficed to call forth the reaction one might be inclined

to say that there was a unilateral hyperesthesia or hyperalgesia. Yet several of these animals, notably those which had been friendly and gentle before the operation, made a practice of rubbing the ipsilateral sides of their bodies against one's ankles or any available inanimate object. The relatively strong mechanical stimulus which they thus applied to themselves never evoked the slightest display of rage or discomfort; on the contrary, it induced the usual feline signs of keen enjoyment. The adequate rage stimulus was always one which was *actively applied* by some external agent. Over the ipsilateral half of the body a slight tactile stimulus sufficed. It is especially noteworthy that the full display of fury, consisting of a vigorous attack upon the immediate source of the stimulus, could be induced from the contralateral half of the body by a degree of nociceptive stimulation which, in the preoperative state, would have produced nothing more than a mild protest. In view of these facts this rage response cannot be attributed to a mere state of cutaneous hyperesthesia or hyperalgesia. Our observations indicate that the threshold for the rage reaction itself was somehow greatly lowered by the unilateral cerebral removal and that the existence of this condition depended upon the integrity of the contralateral cerebral cortex; in cat 244 removal of the latter abolished the response as such. In each of the seven animals the response was temporarily extinguished when signs of fear were induced, and in cat 244 it could not be evoked during oestrus, and during the latter part of pregnancy it disappeared only to return shortly after parturition.

These observations have confronted us with a neurological problem of much interest and we have already devoted no little effort toward its elucidation. Despite the preparation of many cats which have long survived unilateral removals of different amounts of cerebral tissue we have been unable to determine precisely how much of the forebrain or what specific part must be removed or destroyed to induce this excessive rage response. It has occurred in four unilaterally hypothalamic preparations, but not in several others which had been subjected to very nearly the same operation. It failed to occur in four unilaterally decerebrate cats and the condition has not been encountered in a series of some thirty animals lacking the neocortex or all cortex of one hemisphere. The investigation is being continued.

(2) *A Comparison of the Rage Reactions of Acute and Chronic Decorticate Cats*

In the acute experiments on sham rage (1) the animals were tied in the dorsal decubitus on an animal board. This restraint, imposed in order to record arterial pressures and heart rates, doubtless played a rôle in the development of the activity. Although the capacity of those animals to exhibit signs of fury under other conditions was not fully explored, it was found that freeing them did not necessarily abolish the display. In the study of the four surviving decorticate

cats it was found that restraining them on an animal board evoked in each case a reaction which was identical in every detail with the sham rage of the acute preparations.

In certain respects the conditions for the development of the rage responses of the two types of animals were dissimilar. In none of the four surviving cats was it possible to elicit any signs of anger immediately upon their emergence from the anesthesia under which the final cerebral ablation was performed. The capacity developed only after a postoperative period of from one to two weeks. On the other hand, the sham rage of the acute experiments almost invariably began within thirty minutes after the removal of the ether. Since the operations on the group of chronic cats were carried out under sodium barbital or dial (Ciba), it is possible that the long period of narcosis (two or three days) may account for the delay.

One purpose in preparing the chronic animals was to test the hypothesis that the cerebral cortex normally holds in check the hypothalamic mechanism which elaborates the bodily expression of rage. But the results are not conclusive in respect to this point. In the case of cat 103 there were fluctuations in the ease with which the typical behavior could be induced. Her tendency to react to a given rage stimulus was sometimes greater, sometimes less than before decortication. During the fourth and fifth weeks of her survival cat 228 displayed anger under conditions (brushing her back, lifting her gently from the cage) which had proved ineffective as rage stimuli before the final cerebral ablation. The oversensitivity and overactivity were very prominent in No. 313, but not in No. 244. The gradual regression of the rage reaction in No. 228 is of interest, but it does not seem possible to explain the phenomenon on the basis of any known facts. Although some secondary degenerative process may have been responsible, it is certain that degeneration of all severed nerve fibers had taken place before the change began. The animal was essentially a hypothalamic preparation, and if one assumes that the early excessive rage reaction was due to the release of a hypothalamic mechanism from some higher control, one must make further assumptions to explain the regression of the response. It may well be that under normal conditions the part of the forebrain which had been removed contributes excitation as well as inhibition to the hypotha-

lamic mechanism which is responsible for the elaboration of the rage reaction. However, until further evidence becomes available, it is useless to enter into a discussion of this question.

(3) *Expression of Fear*

On the eleventh postoperative day while cat 103 was being observed in a large open space, it happened that the exhaust of an autoclave situated in an adjoining room was opened. The moment the loud noise of escaping steam was heard, the animal suddenly retracted and lowered her head, crouched, mewed and then dashed off, running rapidly in a slinking manner with head, chest, belly and tail close to the floor. After blindly colliding with several objects in her path she came to rest in a corner where she crouched, mewing plaintively. During this activity and for some time afterwards the eyes were widely opened, the pupils were maximally dilated and there was some erection of hair on the back and tail. A few minutes after the noise ceased she resumed her previous behavior—walking slowly about licking the floor. A repetition of the same noise a little later produced the same striking reaction and it was also observed when a very similar noise was made by water running from a tap through a narrow nozzle.

This reaction was frequently obtained in 103 throughout her long survival. Loud noises proved to be the only stimuli capable of inducing it. Many sounds of low intensity (*e.g.*, a low whistle, scraping and clicking noises, the sound of an automobile horn in the distance) caused turning of the head and moving of the ears so that a listening attitude was assumed. It will be recalled that this auditory response diminished and soon disappeared when the stimulus was repeated a number of times, and the same proved true of the quite different response to loud noises. After much experimentation it was found that the most effective stimulus for this fear reaction was a loud blast on a bugle. The loud barking of an excited dog held just in front of the cat only produced crouching and retraction of the head.

In cat 313 a fear reaction of exactly the same nature was repeatedly obtained when a loud blast was blown on a bugle or police whistle. Less intense auditory stimuli proved ineffective. On the eighth day when signs of anger could not be obtained, the fear reaction was evocable and it was repeatedly elicited during the animal's subsequent

career. In 244 the reaction was confined to crouching, retraction of the head, plaintive vocalization, widening of eyes and pupils. This animal never dashed off as did 103. No frank sign of fear could ever be induced in cat 228. When exposed to the noises that proved so effective in the case of 103 and 313, this cat merely twitched the skin of her back and exhibited erection of hair.

When normal cats were subjected to the blast of a bugle or the sound of escaping steam they reacted in very much the same way as did decorticate cats 103, 313 and 244. A few merely crouched with head retracted, eyes wide, and mewed as if frightened and bewildered. Some followed this maneuver by creeping away to hide in a far corner. Others at once dashed off precipitately and made wild attempts to escape from the room as if possessed by the most profound terror. Such observations lead to the conviction that it is entirely correct to describe the similar behavior of the decorticate animals as an exhibition of fear or terror. It is a very specific form of activity that cannot possibly be confused with any other mode of response. The element of escape which was completely lacking in the rage responses of these same animals was a most prominent feature of their fear reactions. Conversely, the element of attack which characterized their exhibitions of anger formed no part of the fear response.

These experiments show conclusively that fear may be displayed after removal of neocortex and much of the rhinencephalon, but they fail to delimit the subcortical region responsible for the display. Of some interest in this connection is the negative result obtained in cat 228. While that animal lacked all but a shred of the striatum and her thalamus proper had been almost entirely ablated, these structures were only partially injured in the animals that gave a positive result. At first sight these facts suggest that striatum or thalamus or both are essential for the production of the fear reaction. But when one considers that the adequate stimuli were auditory, a more cogent explanation comes to mind. In 228 the medial geniculate bodies and their thalamic connections had been removed, whereas these important parts of the central auditory apparatus remained wholly intact in 103 and 313. In 244 whose fear reaction was somewhat less pronounced, one medial geniculate had been extensively damaged. There is nothing in these results to suggest that the display of fear by

decorticate animals is not dependent on the hypothalamus. Although in 228 this region was left intact except its rostral part on the right side, it had been disconnected from the main ascending auditory pathways. The nature and position of the central mechanisms concerned in the production of fear responses remain to be elucidated.

(4) *Sexual Behavior*

The oestrual behavior displayed by cat 103 has been described (p. 80). This was the only instance of well organized sexual activity which occurred in the four animals (all females) after their final cerebral operations. It is also the only instance of oestrus in cats without neocortex so far reported (*cf.* Rioch and Brenner, 32, and Bard, 4). As such, however, it is positive proof that spontaneous oestrus can occur in the absence of neocortex. The observation suggests that the specific behavior pattern characterizing oestrus in cats is elaborated by subcortical mechanisms. Some recent experiments (5) have shown that typical oestrual behavior may be provoked in wholly decorticate cats by administration of oestrogenic substances.

(5) *Signs of Pleasure*

Many persistent attempts were made to evoke signs of pleasure in the four "decorticate" cats. With a single exception these efforts were entirely unsuccessful. When their backs were stroked the animals responded by executing the excessive licking movements of head and tongue, which were characteristically induced by any gentle cutaneous stimulation (see below). Rubbing the sides of their heads sometimes induced deviation or turning of the head against the stimulus, but this was usually followed by attempts to scratch the stimulated region with the ipsilateral hindfoot. The response of the head was therefore probably nothing more than a part of the scratch reflex. Purring was heard in one cat, No. 244, and only on one occasion. While lying on a soft cushion she purred in normal fashion for a few minutes while thermocouples were applied to the skin of her flank for the purpose of measuring cutaneous temperature. Following this observation she was repeatedly subjected to the same comfortable conditions, but it proved impossible to provoke the response a second

time. None of the other cats of this group ever purred or showed the slightest sign of enjoyment when made comfortable and petted.

In view of the observations of other investigators it appears certain that signs of enjoyment may be displayed in cats from which all or nearly all neocortex has been removed. The cat prepared by Schaltenbrand and Cobb (34) purred while eating and in response to being petted or brushed. In that animal, however, there remained certain fairly extensive fragments of neocortex, some of which were undoubtedly in functional connection with the rest of the brain. Rioch and Brenner (32) have recently studied seven cats in which all neocortex had been extirpated except a few small fragments attached to the presubiculum and to the septum. Two of these animals purred normally and vigorously on being stroked and fondled; two others gave a definite appearance of enjoyment when fondled while being fed, but never purred; three failed to show any behavior interpretable as an expression of pleasure. Rioch and Brenner point out that there was a definite correlation between the pre- and post-operative dispositions of their cats; that those which showed signs of pleasure after decortication had been friendly and tractable when normal, while the others which did not respond in this manner postoperatively had been bad-tempered and resisted handling of any kind. On comparing such findings with the study of the four cats of the present report it might be concluded that in the absence of the neocortex the rhinencephalon tends to elaborate behavior which simulates the normal expression of pleasure.[6] In considering these facts it is well to bear in mind that purring in normal cats is not invariably an indication of pleasure. As one of us has pointed out elsewhere (4), it is not uncommon to hear it in cats which are agitated or restless and occasionally it accompanies signs of savageness. It is only when purring accompanies postures or movements indicating pleasure that it is safe to say that it signifies satisfaction or enjoyment.

[6] One of us (P. B.), however, has recently observed most definite pleasure reactions in a cat from which, in addition to all neocortex, the hippocampus and pyriform lobe were removed on each side. The animal regularly purrs in response to being stroked or fed. When her back is stroked she not only purrs but arches her back in a gesture which, in normal cats, suggests pleasure. When she is suspended with legs free, petting will frequently bring on purring accompanied by alternate movements of the forelegs with spreading of the digits at extension.

(6) *The Licking and Biting Response to Cutaneous Stimulation*

The stereotyped licking which can be routinely elicited in decorticate cats by rubbing or scratching them was noted by Schaltenbrand and Cobb (34) and a similar reaction in the decorticate dog was described by Goltz (16). The reflexogenous zone is extensive; it includes the neck, shoulders, back and genital regions. "Local sign" is present in a general way, but the mouth and tongue never quite reach the exact point stimulated (see p. 79). There is a tendency, when the stimulus is applied to or near the midline, for the head to be retracted as it is lowered so that the licking is directed towards the chest and forelegs. When the stimulus is more intense, *e.g.*, scratching, the licking frequently changes to biting and self-inflicted wounds may result.

The licking response as seen in decorticate animals is apparently of the nature of a release phenomenon, *i.e.*, a reflex activity which, after removal of the cortex, is either released from normal inhibition, or is so dissociated from the normal concomitant reactions that it can be elicited readily and alone, rather than being obscured in a complex reaction pattern. On the basis of careful observation on numerous normal cats over long periods of time and under varying conditions, which included oestrus, gestation and the rearing of young, it is clear that this reflex plays a rôle in the feeding, cleaning, oestrual and maternal behavior patterns. The data available, however, do not permit any more definite conclusions to be drawn.

(7) *Cleaning Reactions*

It was necessary to brush the coats of all four cats regularly and to supplement this treatment with occasional baths to keep them from becoming matted and filthy. Such cleaning reactions as were present were merely fragmentary and quite inadequate to maintain the normal condition of the fur. In this connection it is of interest to point out that evidence is available which indicates that the typical feline care of the coat is dependent upon the cerebral cortex, mainly upon the portion lying rostral to the ansate sulci. The same failure of the four cats here described to clean themselves effectively was equally well exemplified by five other cats which lacked the entire neocortex of one hemisphere and the pre-ansate cortex of the other. Five animals which survived for many months bilateral removal of cortex rostral

to the ansate sulci were almost as deficient in this respect as the wholly decorticate cats. That this deficiency in the latter group of animals was not the result of a considerable reduction in the total amount of cortex is shown by the fact that two other animals from which all cortex except the frontal pole of one hemisphere had been removed spent much time licking themselves in normal fashion and kept themselves extremely neat and clean. This point has been mentioned elsewhere in a discussion of the functioning of small cortical remnants (3).

Postprandial nose and chop licking occurred regularly in all four cats. This was usually vigorously performed and was continued much longer than in normal cats, but was neither as well coordinated nor as effective as in the latter.

During the first year and a half of her postoperative life cat 103 frequently licked her chest and the upper part of her forelegs. On one occasion she was seen to lick as far caudalward as her shoulder. Cat 244 spent much of her time licking her left shoulder and foreleg while lying on her right side, with the result that this part of her coat remained clean and smooth. In neither case was this behavior correlated with the presence of dirt.

During the periods when cat 103 was in good condition and under circumstances in which she was not over-active or disturbed, the typically normal reaction of raising and shaking the foot could be routinely elicited by wetting the paw. This also occurred when she accidentally stepped in water spilt on the floor. Occasionally the reaction stopped in its first phase and she would stand for a considerable time with the wet foot held quite motionless in the air. On one occasion, while eating a mixture of salmon and milk she stepped into the dish with her right foreleg. Eating immediately stopped, the head was elevated, the foreleg raised by flexion at the elbow and the foot pads turned medially. In a few moments she started licking the pads and wrist most vigorously. This was continued for some time with interruptions during which the head was moved up and down and from side to side in the air. After approximately ten minutes the foot was lowered and eating continued.

On several occasions when a small clip was attached to the hair of her ear, cat 103 first twitched the ear (pinna reflex), then rubbed that side of her head on the floor and finally raised her forepaw and with it

rubbed the top and lateral aspects of her head while rotating it to the same side. About a year after the second operation this cat would bring her forepaw to the side of her face and rub it when her eye was touched. Cat 244 would at times "wash her face" in a clumsy and incoordinate manner. She would start licking, rotate her head to one side and then raise the ipsilateral foreleg and make rubbing movements which were eventually applied to the head and face.

All four cats assumed the normal postures on defecation and micturition, but these functions were rarely carried out without soiling either the legs or tail. On one occasion when cat 103 was lifted away from her feces and placed on the floor, she turned and made digging and scraping movements with her forelegs. This was the only instance of behavior resembling the normal act of "burying the feces" noted in these cats.

(8) *Locomotion and Posture*

(a) *Locomotion.* In cats 103, 313, and 244 locomotion was occasionally carried out in a manner which could be described as wholly normal. Commonly, however, it presented certain features which suggested either a deficiency of execution or an admixture of postural defect. There was a tendency to carry the head low. On starting to walk or when progressing slowly, these animals sometimes stepped on the dorsum of a forefoot, and the hindlegs stepped from a wide base. When the rate of progression was slow the legs tended to be circumducted and each step was a little retarded at its inception. With increase in pace these peculiarities largely disappeared. The greater sluggishness and more strikingly abnormal locomotion of cat 228 has already been described (p. 91).

(b) *Attitudinal Abnormalities.* In an earlier report (3) it was pointed out that one of the most obvious abnormalities of these four cats was their tendency to assume peculiar attitudes of the legs while standing, sitting or crouching. They were frequently found exhibiting crossing, abduction or backward displacement of the hindlegs. The abduction was usually the result of an uncorrected sliding of the foot away from its normal position. A premature cessation of movement often produced forward or backward displacement of a leg; for example, walking frequently ceased abruptly just as a hindleg had com-

pleted the forward phase of a step, whereupon the foot would remain too far advanced and this abnormal position was often held after the animal had settled into a squatting posture. Similarly, a prematurely arrested act of turning to one side often gave rise to crossing of the forelegs. These strange postures and attitudes were sometimes maintained for long periods. Dusser de Barenne (12) stated that passively imposed abnormal positions of the feet were less rapidly and less completely corrected by his decorticate cats than by normal animals This observation was repeatedly confirmed in the case of each of our cats. The greater prominence of these abnormal attitudes in cat 228 has been mentioned. It should be emphasized that this may be attributed to the fact that she moved about less than the other cats and so spent more time in postures favoring abnormal attitudes. Elsewhere (3) one of us has indicated that these abnormalities were largely due to deficiencies of the placing and hopping reactions which, as Rademaker (29) has shown, are important factors in the maintenance of normal standing. An account of the nature and restricted localization of the cortical control of these postural reactions in cats and rats has been given by Bard (3) and by Bard and Brooks (6). In the cat the placing reactions which are evoked by surface contact and some which are at least partly due to proprioceptive stimuli are entirely dependent upon cerebral cortex (Fig. 26). After removal of cortex, imperfect proprioceptive correcting movements of the legs and a few hopping reactions which are retarded and hypometric can still be obtained. It appears therefore that these latter responses possess a modicum of effective subcortical control. It is of interest that in the four cats with different injuries and removals the residues of hopping and placing reactions were equal.

(c) *Righting.* When placed on their sides or backs each of the cats showed a quite normal ability to get to a standing, squatting or sitting posture. There were no differences among the four animals in this respect. We did not make any analyses of the several righting reactions, since Dusser de Barenne and Magnus (13) have reported the results of a detailed examination of these responses in two cats, one without neocortex and one lacking all cortex, which were prepared by Dusser de Barenne. Although our animals righted themselves very well when in contact with a supporting surface, they showed a marked

deficiency in turning over in the air when dropped back down. The normal cat allowed to fall in this manner turns at once and lands on its four feet even when the fall is one of only a few inches. The four subjects of our study accomplished this maneuver only when dropped from a height of several feet. Occasionally they did not turn in the course of a fall of as much as four feet. The protocols published by Dusser de Barenne and Magnus show that their cat without neocortex was also tardy in turning during a fall, while the wholly decorticate cat did not turn when tested seventeen and seventy-one days after the final cerebral operation. Bilateral labyrinthectomy abolished the response in the first cat. In spite of the fact that the decorticate cat rights its head when held in the air by the pelvis, the deficiency of the response during falling indicates that removal of cortex definitely raises the threshold of the labyrinthine righting reaction. This abnormality in the decorticate cat can scarcely be attributed to absence of the optic righting reaction, for blindfolding the normal animal or enucleating its eyes does not impair to any marked extent the response on falling. In this connection it may be stated that our observations show that another labyrinthine reaction, the "Sprungbereitschaft" of Magnus, has a higher threshold in the decorticate than in the normal cat. Evidently the cerebral cortex in this species facilitates certain labyrinthine reactions which are actually elaborated by subcortical mechanisms.

(d) *Decorticate Rigidity.* All four cats exhibited a nearly normal distribution of muscular tone while standing, sitting or crouching. The legs of each, however, became rigidly extended and strongly resisted passive flexion when the animal was held suspended in any position (Figs. 26, 27). The intensity of this extensor hypertonia was comparable to that of the average decerebrate preparation. Unlike decerebrate rigidity, however, it was revealed in full strength only when the animal's feet were freed from the function of supporting the weight of the body. Thus it appeared in a hindleg that was held forward along the side of the body as the animal squatted on the other three legs; it was displayed in legs which were allowed to hang over the edge of a table upon which the animal rested; and it was invariably found in dependent forelegs which failed to place when the chin was put on some supporting surface. In the dorsal decubitus it was

usually stronger in the hindlegs than in the forelegs. Characteristically the rigidity of any leg disappeared whenever that member engaged in any phasic activity and its distribution could be modified by the operation of the tonic neck and labyrinthine reactions. Following the first ablation it was found in the contralateral extremities only. This extensor rigidity was of the same intensity in the four cats and remained undiminished throughout their survival periods.

Dusser de Barenne and Magnus (13) have given an account of the postural reactions shown by a cat without neocortex, a decorticate cat and a decorticate dog. They stated that the animals showed no decerebrate rigidity and possessed a "normal distribution of tone." Schaltenbrand and Cobb (34) mentioned that their "striatum cat" exhibited normal muscle tone; nevertheless, they noted contralateral extensor hypertonia after the first cortical ablation. Standing in definite opposition to these reports are the result of the study of our four cats and the observations of a number of investigators (7, 22, 24, 25, 26, 35) who have regularly found definite extensor hypertonia after removal of one or another part of the rostral portion of the canine and feline cortex. In view of these facts it seems proper to describe the phenomenon as *decorticate rigidity*.

The fact that an extensor rigidity may be demonstrated after decortication must be taken into account in any explanation of decerebrate rigidity. The evidence at present available strongly suggests that the latter condition depends upon the integrity and overactivity (at least the unopposed activity) of one or more bulbo-spinal mechanisms, especially of the uncrossed vestibulo-spinal system. It may be regarded as a release phenomenon resulting from the removal of inhibitory influences which emanate from various parts of the brain. The view put forward by Magnus and Rademaker (28) to the effect that decerebrate rigidity in the cat is mainly the result of removal of the red nuclei can no longer be seriously entertained (19, 20). Hinsey, Ranson and McNattin (17) have reported a marked hypertonicity of the limb extensors in acute hypothalamic and thalamic cats. This rigidity was identical with that shown by our four cats as regards intensity and the conditions which determined its appearance and disappearance. It developed when the animals were supported in the

air or slung, with legs free, in a hammock; it disappeared and was replaced by a distribution of tone similar to the normal when the animals crouched, stood or walked. It is evident that this rigidity can be abolished by the subcortical neural mechanisms which elaborate these acts. The decerebrate animal is unable to crouch, walk or engage in normal standing. Its rigidity is therefore very much less subject to inhibition and represents the released activity of an isolated bulbo-spinal antigravity mechanism. Decorticate rigidity, on the other hand, develops only when the subcortical influences which can oppose the antigravity mechanism are not in action. It indicates that removal of a cortical influence is an important factor in the genesis of the extensor hypertonia which ensues upon mesencephalic transection of the brain stem.

(e) *Supporting Reactions.* Each of the cats presented throughout its survival period the apparently paradoxical combination of an extensor rigidity of the legs with a definitely diminished positive supporting reaction. As has already been explained, the extensor hypertonia developed only when the legs were freed from the function of supporting the weight of the body. The abnormal weakness of the supporting reaction was seen during standing. It was most marked in the hindlegs and could be readily demonstrated by loading the back or pressing downward against the lower lumbar portion of the vertebral column. This deficit evidently accounted for the tendency of the animals to stand with hindlegs abnormally flexed. The weakness of the supporting tone of the legs shown by decorticate dogs has been described by Rademaker (29). In three of four animals he found the supporting reaction of the legs very slight when the animals were placed in the dorsal decubitus and he suggests that this position exerts a definitely inhibitory influence on supporting tone. But when placed on their backs our four cats as well as three decorticate dogs, which were employed by Pinkston, Bard and Rioch (27) in a study of temperature regulation, showed, so long as they were quiet, a marked extensor rigidity. Indeed the resistance of the legs, as measured by Rademaker's scale test, was often greater when the animal was placed in the dorsal position than when it stood of its own accord. The negative supporting reaction was in our animals, as in Rademaker's,

definitely elicitable. Passive flexion of the distal joints of a limb exhibiting decorticate extensor rigidity invariably caused relaxation proximally.

Rademaker has pointed out that the magnet reaction, the exteroceptive component of the positive supporting reaction, is poor or absent in decorticate dogs. In normal cats it is extremely difficult to demonstrate the presence of this reaction. Accordingly, it does not seem possible to account for the weakened supporting reaction of decorticate cats on the basis of a weakened magnet reaction. The experimental facts suggest that although removal of cortex allows hyperextension of limbs, which are not engaged in standing or phasic movement, it somehow produces a deficiency of the extensor component of the positive supporting reaction when that response is evoked by placing the foot on the ground. It must be admitted that a wholly satisfactory explanation of these phenomena is not yet available.

(9) *Temperature Regulation*

Since apparently normal animals show somewhat different abilities to maintain a nearly constant body temperature in the face of changes in environmental temperature, it is desirable that preoperative studies be made whenever the effects of a cerebral removal are to be tested. Unfortunately, no examinations were made of the temperature-regulating capacities of these cats until after the final cerebral operations. Our interest in this problem developed when it was observed that each of the animals frequently shivered in normal fashion at ordinary room temperatures. We were thereby led to carry out, in collaboration with J. O. Pinkston, a study of the responses to changes in environmental temperature after removal of portions of the forebrain. In that investigation dogs were used primarily, since their reactions to temperature changes proved to be more constant than those of cats. Some observations, however, were made on cats and the report already published (27) includes data obtained on the four animals of the present paper. It is therefore unnecessary to discuss the results in detail.

The most outstanding peculiarity of the thermal responses exhibited by these cats was their excessive reaction to cold. As already mentioned, they shivered at room temperatures which did not produce the response in normal cats. That this was true thermal shivering was

shown by its prompt disappearance when the animal was moved to a warmer environment. In a cold-room (2° to 9°C.) the shivering exhibited by these cats was vigorous and continuous while that of normal animals exposed concurrently was intermittent and less forceful. The over-reaction usually led to some increase in rectal temperature (0.1° to 1.1°C.), but this rise averaged only slightly more than similar increments found in control experiments on normal cats (see Table 2, Pinkston, Bard and Rioch, 27). In the cold-room these cats with extensive forebrain ablations showed much locomotor activity, but in spite of the muscular exercise they continued to shiver vigorously. When they were removed to a hot-room the shivering and the tendency to move about disappeared quickly. In a moderately cold environment (*e.g.*, 15°C.) the cats usually squatted in a hunched-up posture with their forepaws tucked under their chests. On the other hand, at high temperatures they tended to stretch out on their sides thus exposing a large surface for loss of heat. Even moderate cold caused erection of hair and at very low temperatures this specific reaction was very marked.

A few measurements of surface temperatures indicated that the cutaneous vessels were in a state of chronic dilatation. This phenomenon was more thoroughly studied in dogs, and in that species it seems clear that unilateral decortication or merely removal of pre-ansate cortex on one side produces a contralateral cutaneous vasodilatation and some failure of the vasoconstriction which normally occurs on exposure to cold. In time these deficiencies became less distinct. It is possible that the excessive shivering of the decorticate animals was in part the result of an abnormal condition of the skin vessels.

The capacities of the four cats to withstand high environmental temperatures were not fully explored. Since they had been prepared for other purposes it was deemed inadvisable to subject them to the risk of prolonged exposures to heat. We observed, however, that when by chance the temperature of the environment became sufficiently high these cats did engage in true panting (shallow polypneic breathing with mouth open and to-and-fro movements of the tongue synchronous with the respiratory excursions). Indeed they sometimes panted at temperatures which did not evoke the response in normal cats. In spite of our relatively few observations it became

clear enough that in this respect the cats differed from the dogs which had been subjected to essentially the same cerebral ablations (*cf.* 27). When the latter preparations were exposed to thermal conditions that had regularly and promptly induced true panting before decortication, they showed only a slow type of hyperpnea which began after the rectal temperature had risen. Ordinary experience has taught that normal cats do not pant at environmental temperatures which produce the phenomenon in the majority of dogs. In terms of the thermal environment the respiratory response of the dog to heat has a lower threshold than that of the cat. In the dog decortication alters the quality of the response and raises its threshold; in the cat such cerebral ablation does not disturb the mode of the response and may even lower its threshold. Normal dogs usually begin to pant before any rise in rectal temperature has occurred. The reaction may be referred to a stimulation of cutaneous receptors and has been termed reflex panting (Richet). It is not entirely certain that cats ever pant in response to a purely peripheral thermal stimulus, but further work must be done before the neural mechanism of thermal panting in these animals can be accurately described. It can be asserted, however, that the decorticate cat in the chronic condition is able to pant in response to external temperatures which do not provoke the reaction in its canine counterpart. Since a rise in blood temperature can evoke true polypneic panting in dogs during the acute stage following decortication, it has been suggested (27) that the failure of this response in chronically decorticate dogs is due to the secondary degeneration in the thalamus which invariably takes place after removal of cortex. The occurrence of thermal panting in surviving decorticate cats indicates that the central machinery involved in this response has not the same localization in the two species.

Under ordinary conditions all four cats maintained their body temperatures within the normal range (37.4° to 39.0°C.) and withstood exposures to cold (0.6° to 10.0°C.) for long periods (1 to 6 hours) with very small changes in rectal temperature. The actual data have been published elsewhere (27). As already indicated, the abilities of these animals to maintain normal body temperatures on exposure to heat were not investigated in any detail and exact figures cannot be given. It can only be said that they showed no marked deficiencies. Cats

103, 244 and 228 lived in good health during periods of intense summer heat when the temperature of the animal quarters frequently reached 100°F. The fact that no differences in temperature control were noted between the four cats suggests that in the absence of the neocortex and part of the rhinencephalon the striatum plays no significant rôle in temperature regulation.

III. CORRELATION OF THE ANATOMICAL AND PHYSIOLOGICAL FINDINGS

The neopallium was, practically, entirely removed in all four of the preparations, but they differed considerably in the extent of the destruction of the basal ganglia and of the olfactory brain. Interest in the anatomical localization of function in the present series, therefore, centers in these regions.

On general examination of the data one is at first struck by the negative rather than the positive findings. Thus in all four animals there was complete loss of the preoperative "personality" and the responses to the external stimuli which could be received became entirely stereotyped. Since the striatum was only moderately damaged in cat 103 and was entirely absent in cat 228, one may conclude that, in the absence of the neopallium and the major efferent systems of the hippocampus, the striatum plays a very minor rôle in behavior. There is no evidence in this material suggesting that it is a center for the elaboration of "emotional" activity. Similar conclusions are to be drawn from the data on the "licking" responses. It is possible that the sluggishness of cat 228 was related to the absence of striatum, but, as suggested below, this peculiarity may have been due to a lack of important afferent systems. Similarly, the data on the postural reflexes (righting reflexes, hopping and placing reactions, etc.) indicate again that, in the absence of the neopallium, the striatum and the medial basal olfactory areas play no rôle in elaborating or controlling these reactions.

The differences in the "feeding" reactions, however, show a certain degree of correlation with the extent of the injury to the olfactory brain. Thus cat 103, with both of the medial and one of the lateral olfactory tracts present and with the basal olfactory areas of one side more or less intact, responded to odors, ate spontaneously and walked about sniffing at the floor when "hungry," *i.e.*, when food had been

withheld for some time. The spontaneous eating occurred when the food was placed in front of her and was apparently a response to olfactory stimuli. Cat 313 differed anatomically in that the olfactory stalks were cut. There were no responses to odors, but she readily ate of her own accord after having tasted the food and, when "hungry," walked restlessly about licking the floor. Cat 244, with more extensive damage to the basal olfactory areas and striatum, failed to show the sniffing and licking reactions during "hunger," although a certain amount of over-activity in the form of walking took place. Spontaneous eating in response to taste stimuli was present, but considerably less marked than in cat 313. At the extreme was cat 228. Eating occurred only when food was actually placed in the mouth and no spontaneous effort was made to acquire it. Here the chewing and swallowing, probably better described as "a bite and gulping," apparently occurred in response to the tactile sensations from the mouth. Although these data do not give any discrete localization of particular reactions, it is quite clear that the basal olfactory areas together with the associated ventral portions of the striatum and the lower centers with which they are connected, namely, the hypothalamus, subthalamus and reticular substance of the brain stem, are capable of elaborating feeding reactions of a highly complicated type. Post-prandial nose- and chop-licking was very pronounced in all four cats, indicating that it is a function of lower centers. The extent to which it was carried suggested that there may have been some "release" from higher control.

The differences noted in the behavior of the four cats can to a considerable extent be correlated with differences in loss of afferent pathways. Four examples of such correlations may be mentioned. (a) The very low threshold for the "rage" reaction in 313 may have been due to the fact that in this animal the thalamus was only very slightly injured operatively and consequently the connections from the somatic afferent pathway to the hypothalamus were not interfered with. (b) In 228, as noted above (page 90), the auditory paths had been interrupted with the destruction of the medial geniculate bodies, and in this animal the fear reaction to a loud noise and spatial discrimination to a scratching sound were absent. Her only response to noise was a twitching of the panniculus carnosus of the back and a

certain amount of pilomotor activity. (c) Cat 228, with the optic tracts cut and injury to the rostral part of the mesencephalon bilaterally, had fixed, dilated pupils and showed no visual responses whatever, in contrast to the other three cats which had normal pupilloconstriction and also blinked when a bright light was flashed into the eyes. (d) It is noteworthy that cat 228, with the most extensive thalamic lesion and with the interruption of the olfactory, visual and auditory pathways, showed the least amount of spontaneous activity of all of the animals.

Two reactions in cat 244 were unique and no anatomical correlation could be established: on one occasion after the second operation she was heard to purr on being petted, and throughout her postoperative course she licked her left shoulder and foreleg.

SUMMARY

Four cats with approximately symmetrical forebrain ablations have been studied. The neocortex was removed in each case, but different amounts of paleocortex and brain stem were ablated in the separate animals. The operations were carried out aseptically in two stages, following which the animals were studied for long periods (28 months, 6 weeks, 11 months and 13 months, respectively). The brains were sectioned serially and examined microscopically. The anatomical observations have been diagrammatically summarized (Fig. 25). An attempt has been made to correlate, as far as possible, the anatomical and physiological findings (p. 115).

Particular attention was paid to types of behavior which in normal cats are indicative of emotional excitement. In this category three distinct reaction patterns were found in the experimental preparations. These were expressions of rage, fear and sexual excitement. The first has been noted by earlier investigators of the behavior of decorticate carnivores, but the other two have not heretofore been described.

The rage reaction could be evoked in all four cats by appropriate stimuli. Its characteristics have been described (p. 94) and its relation to sham rage in acute preparations discussed (p. 99). In one animal a peculiar and very vigorous rage response developed after the first intracranial operation; it was elicited by lightly touching the side of the body ipsilateral to the cerebral removal (p. 84 and p. 98).

In three cats a response similar to the normal expression of fear could be evoked by loud, high-pitched noises (p. 101). In the fourth animal, which lacked the medial geniculate bodies, the only responses to this stimulus were erection of hair and twitching of the skin of the back.

One cat without neocortex entered spontaneously into heat and displayed typical feline oestrual behavior. This animal possessed a considerable portion of the rhinencephalon, but the thalamus had been largely destroyed by the ablation.

The peculiar licking response elicited by rubbing the skin, especially of the back and genital region, was actively present in all four cats (p. 105). Certain "cleaning" reactions occurred, but were quite inadequate (p. 105). The typical feline care of the coat fails after ablation of the cerebral cortex. Reference is made to evidence indicating that this depends upon that portion of the cortex which is situated in front of the sulcus ansatus (p. 105).

Postural deficiencies were approximately equal in all four cats. The animal with the most extensive ablation displayed the most abnormal locomotion and the greatest depression of spontaneous activity. Although the positive supporting reaction appeared weak, especially in the hindlegs, when the animals were standing, each cat showed a marked extensor rigidity of the legs when these members were freed from the function of supporting the body. The relation of this decorticate rigidity to decerebrate rigidity is discussed (p. 110).

All four cats maintained their body temperatures within normal limits under ordinary laboratory conditions (18°–38°C.) and withstood exposures to temperatures below 10°C. for several hours with very small changes in rectal temperature (p. 112). The thresholds for both shivering and panting were lower than those of normal cats.

There was apparently a correlation between the extent of the destruction of the rhinencephalon and the degree of deficiency of the feeding reactions (p. 115).

Three of the cats, in which the medial geniculate bodies were present, were able to localize a moderately soft scraping, hissing, or clicking sound. The cat without medial geniculates failed to show this reaction.

APPENDIX

The brains of cats 103 and 228 afforded the opportunity for certain observations of anatomical interest, which, no physiological correlations being apparent, are separately described here.

In both cats the stria medullaris received a large contingent of fibers from the septal nuclei (St. m., Fig. 1). A considerable number of these could be followed up into the remaining fragment of the fornix (F., Figs. 2, 17), where they formed a bundle along its ventral surface. This bundle diminished rapidly in size and did not extend further than the anterior third of the fornix longus. No other myelinated fibers were present in the fornix. The origin of this tract, which is presumably the main fornical component of the stria medullaris, seemed to lie in a nuclear mass continuous with the septal nuclei rostrally and extending dorso-caudalward along the ventral surfaces of the fornices. The reduction in size of the bundle of Vicq d'Azyr in cat 103 may be explained on the basis of loss of descending fibers. Such fibers have been noted by Le Gros Clark (11) in Marchi material after lesions of the thalamus.

The large number of fibers in the anterior portion of the internal capsule which are associated with the striatum is noteworthy. This was well shown in cat 103 (Figs. 1–3). Since the cortex had been removed and all but the medial part of the thalamus either destroyed or secondarily degenerated, the remaining fibers must have been connections between the various striatal nuclei, strio-thalamic fibers and connections between the striatum and the rhinencephalon.

The descending strio-fugal fibers and their relation to the peduncle and subthalamus were also well shown in this series. Although the exact site of origin could not be ascertained, the general course through the anterior portion of the internal capsule (Fig. 2) and then through the medial and latero-ventral parts of the peduncle (Figs. 3–5) was clear. The striatal origin and descending course were demonstrated by the fact that these fibers were absent in the brain of cat 228 from which the striatum had been removed. Proceeding caudalward the bundle became progressively smaller as the fibers turned dorso-medialward into the subthalamus. The exact sites of termination were not

apparent. It may be noted that no specific fascicles or separate bundles were found other than the pallido-hypothalamic tract (see below) and the fibers in the field H_2 of Forel. The latter consisted of fibers at first in the medial portion of the peduncle which turned dorso-medially in the upper part of the mesencephalon and formed a rather diffuse group of fascicles dorso-medial to the peduncle (H_2, Fig. 4). They finally entered the anterior and lateral aspects of the capsule of the red nucleus.

A large number of the strio-fugal fibers ended in the nucleus entopeduncularis. Many of these apparently arose in the caudate and putamen, which is further evidence suggesting that the nucleus entopeduncularis of lower mammals is homologous with the medial part of the globus pallidus of primates.

At about the middle of the nucleus entopeduncularis a small group of well-myelinated fibers turned dorso-medially out of the strio-fugal tract (Tr. pal-hyp., Fig. 4). It could be followed across the rostral part of the field H_1 of Forel and then ventrally into the hypothalamus to the region of the anterior part of the nucleus hypothalamicus ventro-medialis, where the myelin sheaths terminated. The striatal origin and direction of conduction were evidenced by the fact that this bundle was absent in cat 228.

In cat 103 there were no myelinated fibers in the peduncle below the level of the substantia nigra, and in cat 228 none was present even in the upper levels. From this it may be concluded that the peduncles contain no myelinated fibers of subthalamic or lower origin. It would appear to represent the lateral forebrain bundle of lower forms, *i.e.*, the cortico-strio-fugal system.

Special note should be made of the field H_1 of Forel (H_1, Figs. 3–5, 19). This region was equally well preserved in both preparations and showed little, if any, change from the normal. The bundles of fibers could be readily followed from the level of the red nucleus, particularly from the anterior and medial aspects of its capsule, and from the reticular substance of the mesencephalon through the field of Forel to the zona incerta and the caudo-ventral parts of the thalamus. In view of the extent of the forebrain lesion it may be concluded that these fibers belong mainly to ascending systems, *e.g.*, the dento-rubro-thalamic tract, reticulo-thalamic tracts. Descending fibers from

the zona incerta and the reticular nucleus of the thalamus may also be present.

Another subthalamic fiber system which showed very little change was the supra-mammillary decussation of Forel. This was essentially normal in cat 103 and only very slightly reduced in size in cat 228 (D. s-m., Fig. 19). It may be concluded that the fibers are mainly of mesencephalic and subthalamic origin.

The supra-optic commissures were normal in cat 103 (G., Mey., Fig. 3), but in cat 228 Gudden's commissure had been cut with the optic tracts and only two or three fibers of Gansser's commissure could be found. This would indicate that Gansser's commissure is a descending system (15, 18).

A small, discreet bundle of fine to medium-sized fibers (Tr. ped. tr., Figs., 28, 29) extended transversely around the surface of the degenerated peduncle in both preparations. Medially the fibers scattered out in the region between the red nucleus and the substantia nigra at the level of the exit of the oculomotor nerve. The lateral termination of the bundle was at a slightly more caudal level. Here the fibers joined small bundles of similar-sized fibers in the lateral third of the brachium of the inferior colliculus. The course over the peduncle and the medial termination of this bundle identifies it as part of the tractus pedunculus transversus. However, since the bundle was equal in size in both cats 228 and 103, it is evident that the origin of these fibers is other than the cortex, the striatum or the optic nerve (*cf.* 8).

The bundles of fibers in the lateral third of the brachium of the inferior colliculus, of which group the tractus pedunculus transversus seemed to be one component, were themselves part of a more extensive system of fine to medium-sized fibers running over the lateral surfaces of the mesencephalon. Dorsally, this system appeared to connect with the inferior colliculus and with both the superficial and deep layers of the colliculus. The general course was caudo-ventral. A large number of the fibers turned medially, dorsal to the peduncle, into the reticular substance of the mesencephalon lateral and caudal to the red nucleus. Others entered the lateral part of the substantia nigra. Finally, a rather large group ran ventro-caudalward through the lateral margin of the peduncle into the rostral pole of the pontile

nuclei. Cell groups lying lateral to the lateral lemniscus seemed to be associated with this system.

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KEY TO ABBREVIATIONS USED

am., Amygdala
A. p-o., Area pre-optica
A. p-t., Area pretectalis
Aq., Aqueductus Sylvii
Br. c. i., Brachium colliculi inferioris
Br. c. s., Brachium colliculi superioris
C. a., Commissura anterior
Ch. o., Chiasma opticum
C. i., Capsula interna
C. m., Centre median
Col. s., Colliculus superior
Com. h., Commissura habenularis
Com. p., Commissura posterior
Diag. B., Diagonal band of Broca
D. s. m., Decussatio supra-mamillaris
Ent., Cortex cerebri entorhinalis
F., Fornix
G., Commissura supra-optica Gansserii
Gl., Globus pallidus
Hab., Ganglion habenulare
Hip., Hippocampus
H_1, Campus Foreli H_1
H_2, Campus Foreli H_2
Hyp., Hypothalamus
L. m., Lemniscus medialis
L. m. i., Lamina medullaris interna
Mey., Commissura supra-optica Meynerti
N III., Nervus oculomotorius
N. ac., Nucleus accumbens
N. a. m., Nucleus antero-medialis
N. a. v., Nucleus antero-ventralis
N. c., Nucleus caudatus
N. c. l., Nucleus centro-lateralis
N. c. m., Nucleus centro-medialis
N. ent., Nucleus entopeduncularis
N. g. l. d., Nucleus geniculatus lateralis dorsalis
N. g. l. v., Nucleus geniculatus lateralis ventralis
N. g. m. m., Nucleus geniculatus medialis magnocellularis
N. g. m. p., Nucleus geniculatus medialis principalis
N. l., Nucleus lateralis
N. mam. m., Nucleus mamillaris medialis
N. m. d., Nucleus medialis dorsalis
N. p., Nucleus posterior
N. p-c., Nucleus paracentralis
N. p-f., Nucleus parafascicularis
N. p-ol. l., Nucleus parolfactorius lateralis
N. p-ol. m., Nucleus parolfactorius medialis
N. p-t., Nucleus parataenialis
N. r., Nucleus ruber
N. ret., Nucleus reticularis
N. s-g., Nucleus supra-geniculatus
N. st. t., Nucleus striae terminalis
N. sub., Nucleus subthalamicus
N. v., Nucleus ventralis
N. v. c., Nucleus ventralis, pars commissuralis
P. p., Pes pedunculi
Pre-sub., Presubiculum
Put., Putamen
Pyr., Lobus pyriformis

S. n., Substantia nigra
St. m., Stria medullaris
St. t., Stria terminalis
Subic., Subiculum
T. h-p., Tractus habenulo-peduncularis
T. m-th., Tractus mamillo-thalamicus
T. ol. l., Tractus olfactorius lateralis
T. ol. m., Tractus olfactorius medialis
Tr. op., Tractus opticus
Tr. pal-hyp., Tractus pallido-hypothalamicus
Tr. ped. tr., Tractus pedunculus transversus
Tub. ol., Tuberculum olfactorium
Vent. III., Ventriculus tertius
Z. i., Zona incerta

PLATE 1

FIGS. 1 TO 3. Microphotographs of transverse sections through the brain of cat 103. Weigert-Pal. × 4

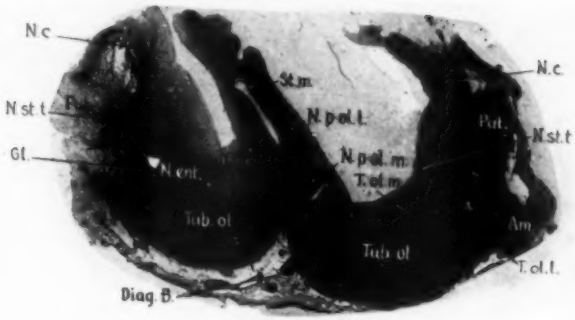

FIG. 1

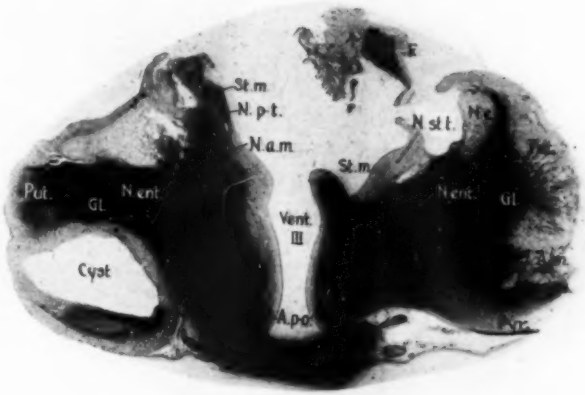

FIG. 2

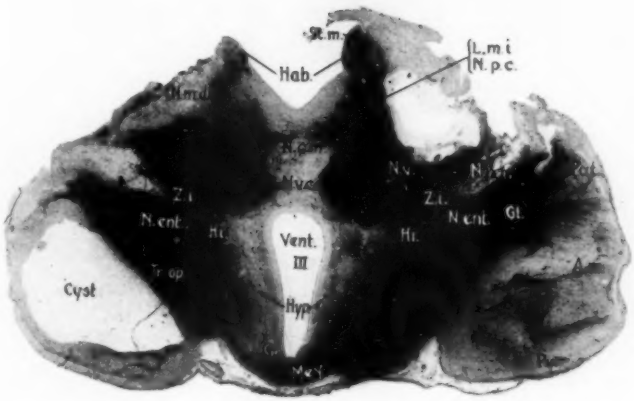

FIG. 3

PLATE 2

FIGS. 4 AND 5. Microphotographs of transverse sections through the brain of cat 103. Weigert-Pal. × 4

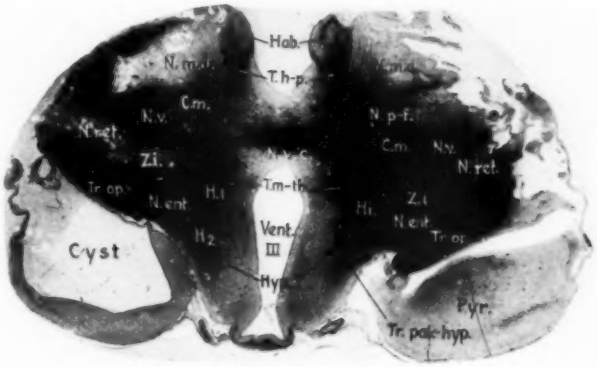
Hab.
N. mot.
T. h-p.
C.m.
N.v.
N. ret.
Zi.
Tr. op.
N. ent
H1
H2
Tm-th.
Vent. III
Hyp.
Cyst
N. p-f.
C.m.
N.v.
N. ret.
Z.i
H1
N. ent
Tr. op.
Pyr.
Tr. pal-hyp.

FIG. 4

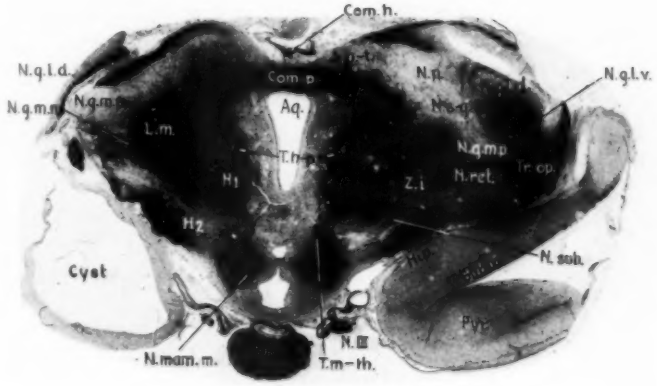
Com. h.
N.g.l.d.
N.g.m.m.
N.g.m.s.
L.m.
Com. p.
Aq.
T.h-p.
H1
H2
Cyst
N.mam.m.
N.III
Tm-th.
N.g.l.v.
N.g.mp
N. ret.
Tr. op.
Z.i
N. sub.
Pyr.

FIG. 5

PLATE 3

FIGS. 6 TO 8. Microphotographs of transverse sections through the brain of cat 313. Thionin. ×4

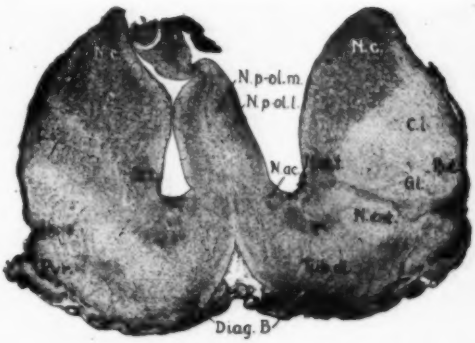

FIG. 6

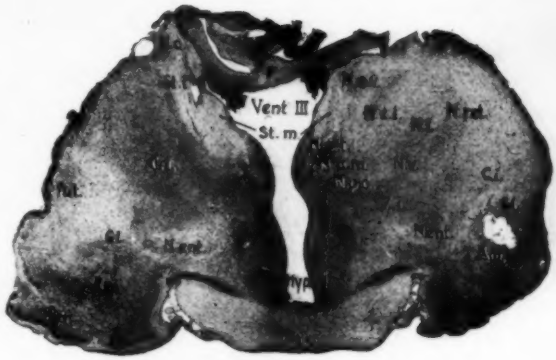

FIG. 7

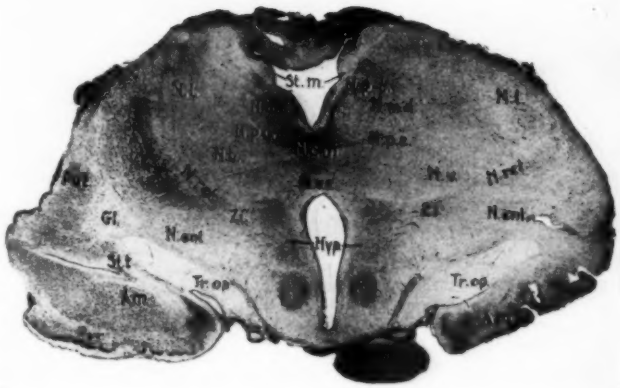

FIG. 8

PLATE 4

FIGS. 9 TO 11. Microphotographs of transverse sections through the brain of cat 313. Thionin. × 4

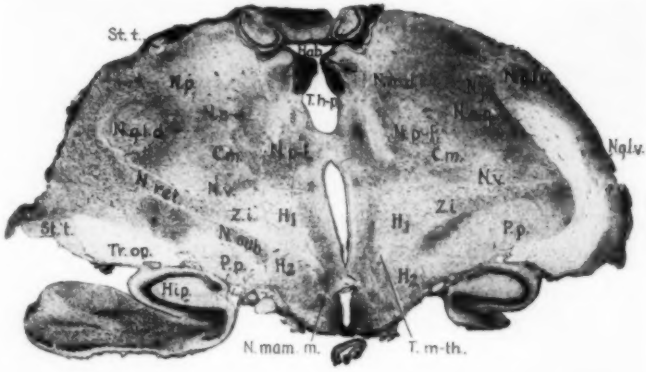

FIG. 9

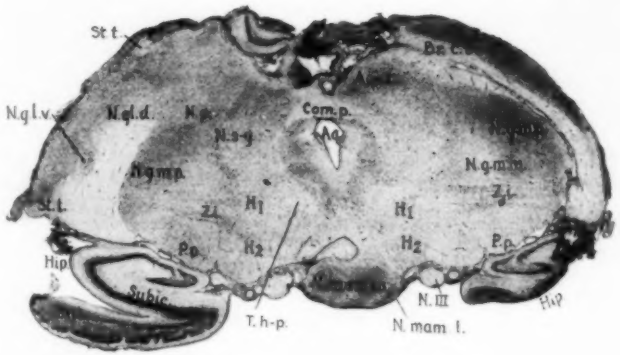

FIG. 10

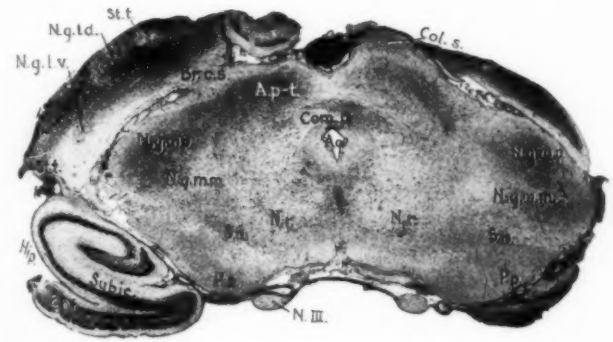

FIG. 11

PLATE 5

FIGS. 12 TO 15. Microphotographs of transverse sections through the brain of cat 244. Thionin. × 4

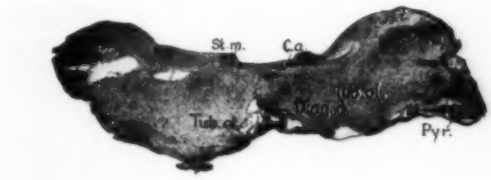

FIG. 12

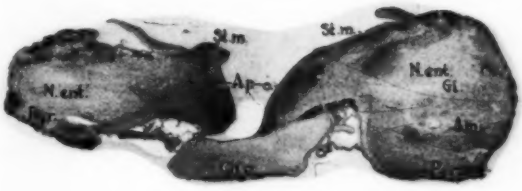

FIG. 13

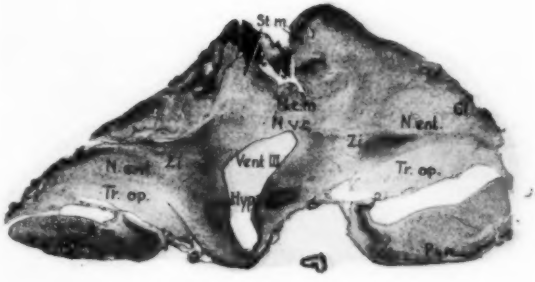

FIG. 14

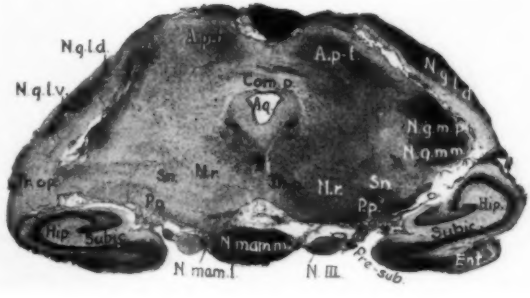

FIG. 15

PLATE 6

FIGS. 16 TO 18. Microphotographs of transverse sections through the brain of cat 228. Weigert-Pal. × 4

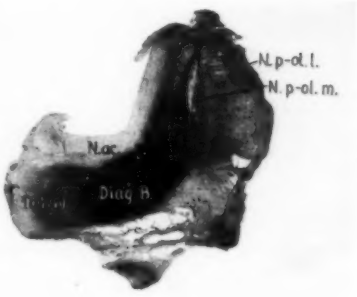

FIG. 16

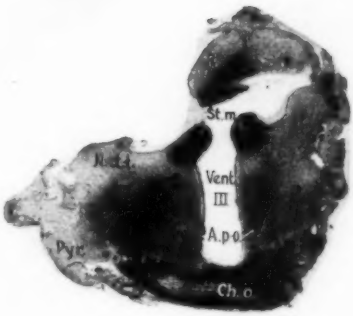

FIG. 17

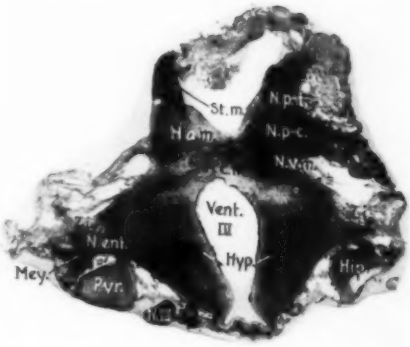

FIG. 18

PLATE 7

FIGS. 19 AND 20. Microphotographs of transverse sections through the brain of cat 228. Weigert-Pal. × 4

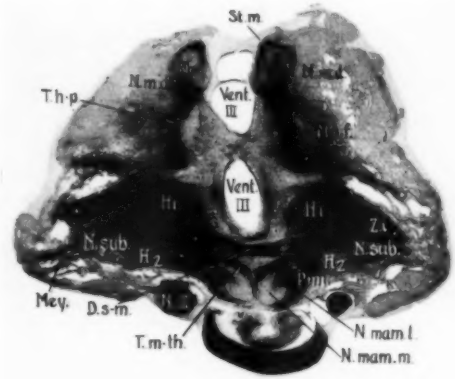
St.m.
Th.p.
Vent. III
Vent. III
H1
H1
N.sub.
H2
Z1
N.sub.
H2
Mey.
D.s-m.
T.m-th.
N.mam.l.
N.mam.m.

FIG. 19

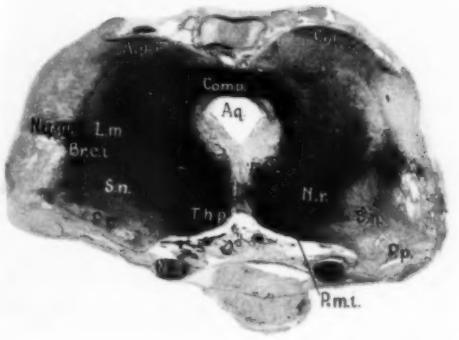
Comp.
Aq.
L.m.
Br.c.t.
S.n.
Th.p.
N.r.
Pp.
R.m.t.

FIG. 20

PLATE 8

FIGS. 21 to 24. Photographs of the dorsal aspects of the brains of cats 103, 313, 244 and 228, respectively. × 1.25

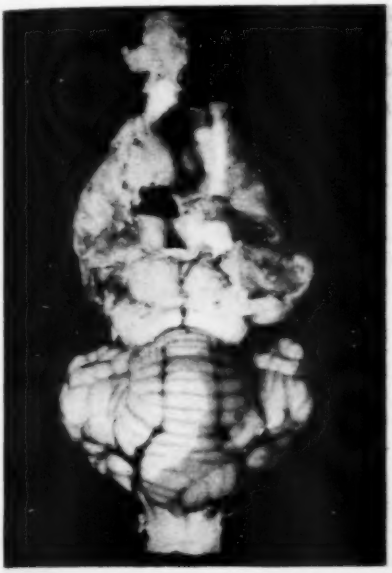

FIG. 21

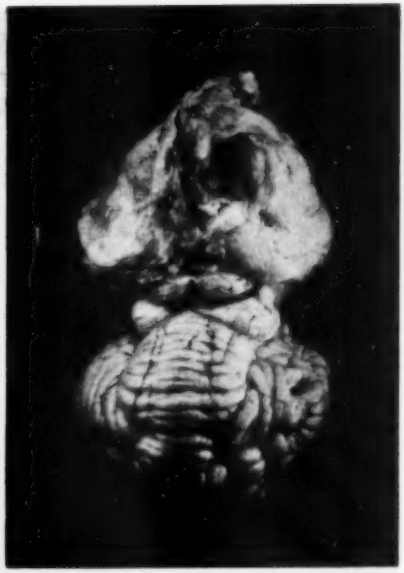

FIG. 22

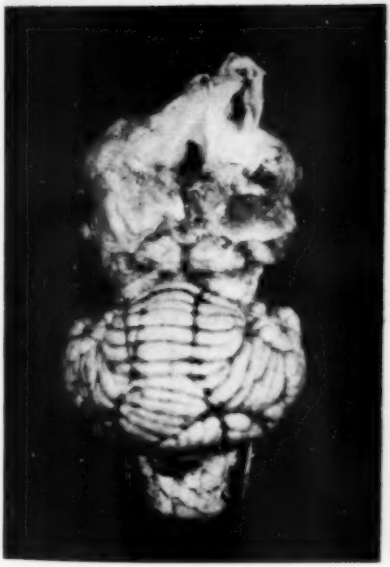

FIG. 23

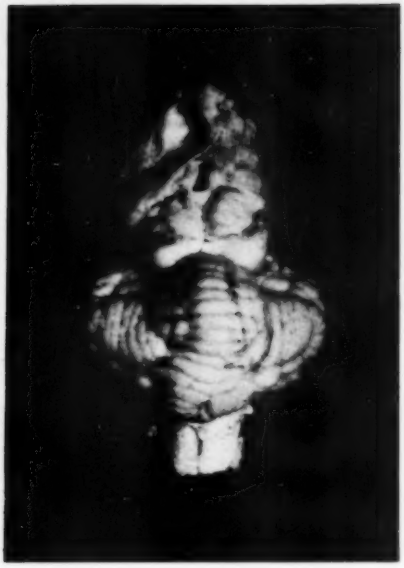

FIG. 24

FIGURE 25

A DIAGRAMMATIC REPRESENTATION, RECONSTRUCTED FROM THE HISTOLOGICAL STUDIES, OF THE BRAINS OF THE FOUR CATS UNDER INVESTIGATION

Key: Solid block: Portions of the brain removed at operation. Cross hatched: Portions of the brain not directly involved at operation, but which showed degeneration or loss of the ganglionic elements. Stippled: Portions of the brain which showed general shrinkage in size, but with normal ganglionic elements. (Possibly due to loss of fibers.) Plain: Portions of the brain which showed no histological changes. *1*, neocortex; *2*, olfactory bulbs; *3*, olfactory stalks; *4*, tuberculum olfactorium; *5*, pyriform lobe and amygdala; *6*, hippocampus; *7*, head of caudate nucleus; *8*, putamen; *9*, globus pallidus and entopeduncular nucleus; *10*, subthalamic nucleus, red nucleus and substantia nigra; *11*, dorsal thalamus; *12*, hypothalamus; *13*, superior colliculus; *14*, inferior colliculus; *15*, tegmentum of mesencephalon; *16*, medulla, level of pons; *17*, cerebellum; *18*, medulla, level of vagal nuclei.

FIG. 25

PLATE 9

FIG. 26. Photograph of cat 244 with her wrists against the edge of the testing table. Note the absence of placing reactions and the extreme extensor rigidity.

FIG. 27. Photograph of cat 244 held in the dorsal decubitus with the legs free. Note the extensor rigidity.

FIG. 26

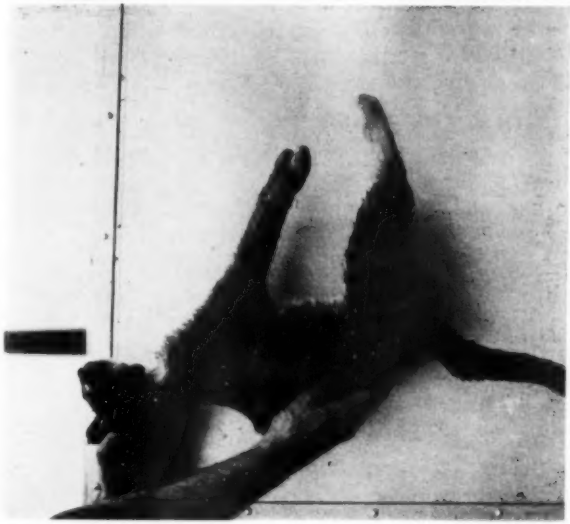

FIG. 27

PLATE 10

FIG. 28. Microphotograph of transverse section through the brain of cat 103 at the level of the red nucleus to show the Tractus pedunculus transversus. Weigert-Pal. × 16.6

FIG. 29. Microphotograph of transverse section through the brain of cat 228 at the level of the exit of the oculomotor nerve to show the Tractus pedunculus transversus. Weigert-Pal. × 16.6

FIG. 28

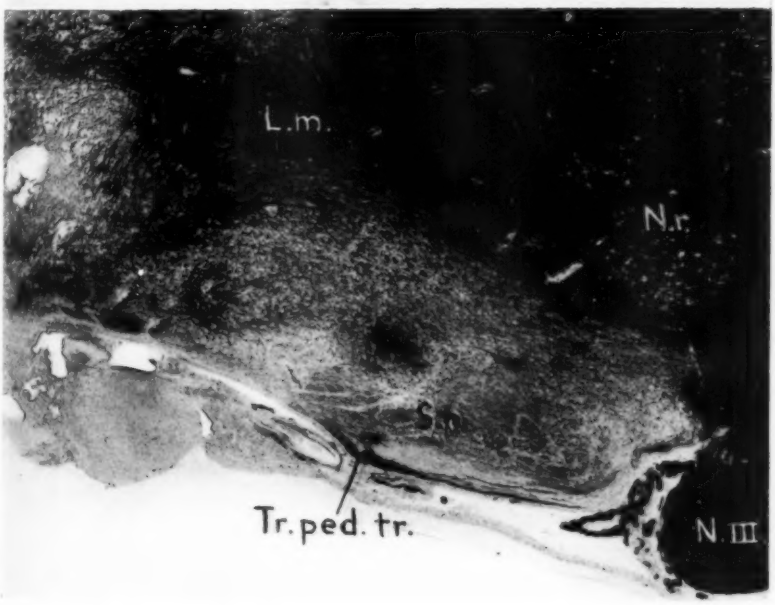

FIG. 29

THE ACTIVATION OF "PRONTOSIL SOLUTION" IN VITRO BY REDUCTION WITH CYSTEINE HYDROCHLORIDE[1]

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From the Department of Medicine, The Johns Hopkins University Medical School

Submitted for publication January 7, 1937

Domagk (1) and Colebrook and Kenny (2) have shown that *Prontosil* and *Prontosil Soluble*, in spite of their excellent therapeutic effects in Beta haemolytic streptococcal infections in mice, have no inhibitory effect upon the growth of these organisms *in vitro*. On the other hand, it has been shown (3) that para-amino-benzene-sulphonamide is active in the test tube as well as in the animal body (4).

Colebrook and Kenny also noted that serum from a normal rabbit which had received a large amount of *Prontosil Soluble* intravenously failed to inhibit the growth of streptococci, but that the serum of patients ill with puerperal sepsis became increasingly bacteriostatic after repeated injections of *Prontosil Soluble*. These observations are interesting, since they suggest that for the activation of *Prontosil solution* "infection with haemolytic streptococci, or changes brought about by such infection are necessary" (3).

In a previous paper (3) we presented evidence that this activation of the disodium salt of 4′-sulphamido-phenyl-2-azo-7-acetylamino-1-hydroxynaphthalene-3,6-disulphonic acid (*Prontosil*—2.5 per cent solution) was attributable to a reduction of the dye in the animal body. The purpose of the present study was to see whether this chemical could be reduced *in vitro* and whether the reduced product possessed bacteriostatic powers. If such reduction actually occurred, it seemed probable that the molecule would divide at the double bond and that para-amino-benzene-sulphonamide would be one of the

[1] The *Prontosil solution* was supplied by The Winthrop Chemical Co. of New York City.

[2] This study was supported by a grant from the Chemical Foundation, Inc. of New York City.

products. This would be consonant with the theory of Tréfouël, Nitti and Bovet (4) that, in the animal body, *Prontosil* breaks down and forms para-aminobenzene-sulphonamide. Just as the present study was being brought to a close, an article by Colebrook, Buttle and O'Meara (5) appeared, in which it was briefly mentioned that they had found that *Prontosil* or *Prontosil Soluble* could be reduced *in vitro* with magnesium powder, in a partial vacuum, and that "a substance was produced from the dyes which had an inhibitory effect comparable to that of para-amino-benzene-sulphonamide." A little later in the same article the authors state that their colleague, Dr. Fuller, "has shown that the sulphonamide is produced from *Prontosil* by reduction of the dye in the body."

EXPERIMENTAL

In the experiments to be described it was assumed that with complete reduction 7.3 mgm. of para-amino-benzene-sulphonamide would be produced for every cubic centimetre of a 2.5 per cent *Prontosil solution*. A sufficient amount of the *Prontosil solution* was used, therefore, to give a final concentration of 1/10,000 of the hypothetical para-amino-benzene-sulphonamide. After trying several reducing agents (sodium formaldehyde sulphoxalate and sodium dithionite), cysteine hydrochloride was selected. A final concentration of 1/500 was found to be the most satisfactory. Higher concentrations were in themselves inhibitory to the growth of streptococci and lower concentrations were not sufficiently active as a reducing agent.

Procedure. From 3.7 to 3.9 cc. of broth were placed in each of four Wassermann tubes. To two of them was added 0.1 cc. of the dilution of *Prontosil solution*. To one of these and to a third tube was added 0.1 cc. of the cysteine hydrochloride solution. All four tubes were inoculated with 0.1 cc. of a young (14 to 16 hours) broth culture of a strain of Beta haemolytic streptococci, diluted 1/500,000. Plate counts from this amount of inoculum ranged from 7 to 92 colonies. In practice the tubes were always inoculated before the addition of the cysteine, so that the reducing agent would be exposed as little as possible to the air. They were immediately sealed with vaseline. The protocol of the experiments is given in Table I. In about half of the tests the broth was replaced by 50 per cent normal horse-serum broth. The tests were incubated at 37°C. for 16 to 18 hours. Then they were examined and plates were poured with appropriate dilutions.

TABLE I

Protocol of reduction experiments

SUBSTANCE	TUBE 1	TUBE 2	TUBE 3	TUBE 4
	cc.	*cc.*	*cc.*	*cc.*
Broth (or 50% serum-broth)	3.7	3.8	3.8	3.9
"Prontosil"—2.5% solution—diluted 5.48/10	0.1	0.1	0	0
Cysteine HCl—8% solution	0.1	0	0.1	0
Culture—1/500,000 dilution	0.1	0.1	0.1	0.1

TABLE II

Inhibition of growth of haemolytic streptococci in media containing "Prontosil" solution reduced with cysteine HCl

EXP. NO.	STRAIN	APPROXIMATE NUMBER OF ORGANISMS INOCULATED	MEDIUM	ESTIMATED REDUCTION OF "PRONTOSIL" IN TUBE 1 (16 HRS.)	RESULTING GROWTH, COLONIES PER CUBIC CENTIMETER				DEGREE OF INHIBITION (CF. TUBES 1 AND 3)
					Tube 1	Tube 2	Tube 3	Tube 4	
L	C203	7	Broth	Complete	30,000	63 million	75 million	80 million	2,000 fold
M	C203	92	Serum broth	1/2	70 million	350 million	500 million	350 million	7 fold
P-1	C203	20	Broth	Complete	7,000	100 million	170 million	125 million	24,000 fold
P-2	C203	20	Serum broth	1/4	80 million	320 million	365 million	330 million	4½ fold
T-1	Ellis	30	Broth	7/8	136,000	98 million	41 million	42 million	300 fold
T-2	Ellis	30	Serum broth	1/4	58 million	165 million	330 million	160 million	5 fold

Two strains of Beta haemolytic streptococci were used. One of them, the well known C203, is highly virulent for mice. The other (Ellis) was recently isolated from a patient with scarlet fever and has a very low mouse virulence.

RESULTS

Eighteen tests were made. In all of them some inhibition of growth was noted in the tubes containing reduced *Prontosil*. Examples of the more striking results are shown in Table II. As shown there, *Prontosil solution* after it has been subjected to the action of cysteine hydrochloride inhibits the growth of haemolytic streptococci, whereas neither substance alone is bacteriostatic. There was considerable variation in the degree of reduction of the *Prontosil* as judged by loss of the red colour of the dye. Reduction was never immediately apparent but increased gradually during the period of incubation. It was always better, in 16 hours, in the tubes with the broth base than in the serum-broth tubes. If, however, the serum-broth tubes were allowed to remain longer in the incubator, reduction proceeded to completion. Reduction was not dependent upon the presence of streptococci since it occurred equally rapidly in uninoculated tubes.

There was also some variation in the amount of inhibition shown. Inhibition was always more marked in the broth cultures than in the serum broth. This was true even when parallel tests were run in the two media. We believe that this was due partly to the fact that reduction of *Prontosil solution* is much slower in the presence of serum and partly to the more rapid growth of streptococci in serum broth. There were from two to four times as many streptococci in 16 hours in the serum-broth controls as in the straight broth controls seeded with identical inocula.

The observation that reduced *Prontosil solution* had a bacteriostatic effect upon the growth of Beta haemolytic streptococci *in vitro* led us to test the therapeutic efficacy of the reduced compound in experimental peritonitis in mice. It was found that *Prontosil solution* which had been rendered colourless by reduction had a therapeutic activity in this infection comparable to what would be expected from a solution of para-amino-benzene-sulphonamide of the same concentration.

CONCLUSIONS

Prontosil solution which has been subjected to reduction by cysteine hydrochloride inhibits the growth of Beta haemolytic streptococci *in vitro*.

Reduced *Prontosil solution* is active therapeutically in mice infected with haemolytic streptococci.

It is believed that the substance in reduced *Prontosil solution* that exerts the bacteriostatic action is para-amino-benzene-sulphonamide, but as yet no chemical proof of its nature is at hand.

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2. Colebrook, L., and Kenny, M.: *Lancet*, 1936, I, 1279.
3. Long, P., and Bliss, E.: *J. A. M. A.*, 1937, **108**, 32.
4. Tréfouël, J., et Mme., Nitti, F. and Bovet, D.: *C. r. Soc. de biol.*, 1935, **120**, 756.
5. Colebrook, L., Buttle, G., and O'Meara, R.: *Lancet*, 1936, ii, 1323.

BOOK REVIEWS

Pathological Physiology and Clinical Description of the Anemias. By WILLIAM B. CASTLE and GEORGE R. MINOT. 205 pp. $3.00. (*Oxford University Press, New York, 1936.*)

The present is a period of the opening up of new fields in haematology. The old division into "primary" and "secondary" anaemias, with the emphasis on cytology resulting in a multiplicity of names, is giving place to a system of classification based on a knowledge of the physiological processes and of the factors that influence these processes, an understanding of which in any particular case constitutes the essential diagnosis. Much of the advance in recent years has been the result of the work done under the leadership of the two authors. The book is a pleasure to read as well as a storehouse of facts and should appeal not only to the clinician with his problems of diagnosis and treatment, but also to the student who is groping in the confused mazes of "classical" haematology.

The work is essentially clinical, but as a basis for their discussion of the pathology of anaemia, the authors review in some detail the conception of the "erythron" as recently developed in England. Whether this conception will lead to any advance in the understanding of pathological problems may be open to question, but there is no doubt that it greatly simplifies the presentation of a difficult subject. In general, and possibly it is best in a book designed for the clinician, the emphasis is placed on the known facts and the way in which they fit into an orderly system; the unknown and the controversial are not included in the discussion.

It is unnecessary to review in any detail the various chapters. It is natural that the book should reflect the interests of the authors, and the most outstanding parts deal with "macrocytic anaemias due to deficiency of substances effective in pernicious anaemia," with hypochromic anaemia, and with therapy. The rich field of infancy and childhood is scarcely touched and in that of the haemolytic anaemias there is no advance over the conception of ten years ago.

One of the most difficult problems in haematology is that of classification, especially one that will introduce order into teaching and filing cabinets, and at the same time will not interfere with one's thinking. The authors have attempted one based on etiology and the result is probably as good a practical system as could be devised at the present time. There are one or two faults, however. There is a practical difficulty, for instance, in the separation of the haemolytic anaemias from those with erythroblastosis. The words "due to" preceding "mechanical interference with the blood forming organs" implies more knowledge than we possess; "associated with" would interfere less with freedom of thought; also, not everyone would agree with the inclusion of such conditions as Hodgkin's

disease or Gaucher's disease in this category. "Idiopathic" is too positive a term; it is apt to be misinterpreted, as "primary" was misinterpreted in the past. These seem like minor considerations, but unfortunately names do occasionally have a way of clouding one's understanding, and order, however admirable, can too easily retard progress.

H. W. J.

Elements of Psychology. By KNIGHT DUNLAP. 499 pages. Illus. $3.00. (*The C. V. Mosby Company, St. Louis, 1936.*)

In a new and modernized edition, the author discards psycho-physical parallelism for a concept of consciousness as a reaction system of the whole organism. Thus he comes closer to the psychobiological concept of man's functioning as a whole, whose individual functions are inseparable from the integrated unit. Unfortunately, the presentation, dealing as it does with elements and topics, cannot always adhere to the concept of unity laid down in the first chapter. The factual data are, however, completely and clearly presented, except in the final chapter, where the material on neuroses and psychoses is not only inadequate, but clearly misleading and at variance with modern psychopathological principles. It is a pity that a book which carries psychology a long way forward in a very humanized treatment of aspects of function should limit the integration concept to a mere neurologizing correlation by a central nervous system. None the less, it should be welcomed as marking a tremendous advance over traditional introspective psychology. The presentation is unusually lucid and attractive, and is strongly recommended for students wishing an up-to-date account of the elements of man's mental functioning.

T. A. C. R.

An Introduction to Psychological Medicine. By DRS. R. G. GORDON, N. G. HARRIS and J. R. REES. 386 pages. $4.00. (*London, Oxford University Press, 1936.*)

This textbook for students aims at a general orientation into common psychiatric problems. The introductory chapters deal with the organization of man's nature along the lines of his cognitive, conative and affective components. The psychopathology is presented largely along the lines of psychoanalytic concepts of repression, dissociation, regression and symbolization. Section 3, on the psychoneuroses, and Section 4, on the psychotic reactions, present the usual clinical material, grouped according to the accepted German nosological types, with dynamics rather briefly touched upon. The final section deals with mental deficiency and its legal and social implications, and presents the British law in its relation to mental illness.

The presentation is largely didactic, there being little or no case material, and the discussions are frequently brief and somewhat superficial. Similar material has been more completely presented in the standard British and American textbooks.

T. A. C. R.

A Textbook of Physiology. By WILLIAM H. HOWELL. 13th ed., thoroughly revised. 1150 pp. Illus. $7.00. (*W. B. Saunders Co., Philadelphia, 1936.*)

In the preface to the original edition (1905) of his text, Dr. Howell states that he endeavored to keep in mind two guiding principles: first, the importance of simplicity and lucidity in the presentation of facts and theories; and second, the need of a judicious limitation of the material selected. The present edition continues to exhibit these two ideas. It is one of the most readable of textbooks of physiology, and although many of the recent advances in this branch have been incorporated in it, this edition has only twenty-eight more pages than the former (1933). In fulfilling these conditions, Dr. Howell has maintained his book in its high place among the textbooks of physiology.

C. L. G.

British Masters of Medicine. Edited by SIR D'ARCY POWER. 242 pp. 33 illustrations. $3.00. (*William Wood and Company, Baltimore, 1936.*)

In this beautifully printed volume, the distinguished editor has brought together and revised a series of articles that appeared originally in the *Medical Press and Circular* in 1934 and 1935, describing the lives and contributions of the greater physicians and surgeons of England, Scotland and Ireland from the time of William Harvey (1578–1657) to that of E. H. Starling (1866–1927).

The articles were, in the main, written by persons who have been attached to the great institutions that their heroes made famous. Thus, Harvey is dealt with by Sir Charlton Briscoe, Sydenham by Sir Humphrey Rolleston, Hunter by Sir Arthur Keith, Jenner by Sir Buckston Browne, Bright by Arthur F. Hurst, Addison by Thompson, Stokes by T. G. Moorhead, Simpson by J. D. Comrie, Paget by Sir D'Arcy Power, Lister by Sir St. Clair Thomson, Osler by Mrs. Edith Gittings Reid, and the others by equally qualified writers.

These brief biographical chapters make delightful reading. They bring vividly before us the personalities of the great men described and recount their outstanding contributions; and they are revelatory of the progress made by medicine and science during the past four centuries. The volume will doubtless find a host of readers who can scarcely fail to find in it many incentives to a high order of work.

L. F. B.

A Textbook of Surgery. By JOHN HOMANS, M.D. 4th Edition. 1267 pp. Illus. $8.00. (*Charles C. Thomas, Springfield, Ill., 1936.*)

An excellent book. It is well arranged and the subjects are presented in a concise, logical, and attractive style. The 4th edition contains an additional and valuable section on amputations and plastics. The chapters on antiseptics, sterilization, diseases of the thyroid gland, fractures of bones, and disorders of the sympathetic system have been revised. The last named is presented particularly well. It is untainted by prejudice or over-enthusiasm and affords one of the clearest, most concise, and practical expositions of the subject available. The bibliography is well chosen.

One might perhaps criticize the lack of completeness, inasmuch as such unusual lesions as chylothorax, glomus tumors, etc. are completely ignored, while the details of therapy are in many instances lacking. For these reasons the book is to be recommended more to the medical student than to the practising surgeon.

R. T. S.

The Truth About Bright's Disease. Harvard Health Talks, 19. By WILLIAM R. OHLER. 1st ed., 80 pp. Illus. $1.00. (*Harvard University Press, Cambridge, 1936.*)

With a text covering only 68 pocket-sized pages, and with the aid of two small anatomical diagrams, the author attempts to explain to the layman the modern physician's concept of Bright's Disease.

The author's skillful condensation of his extremely complex subject is partially spoiled by a lack of facility in exposition. The reviewer believes that the layman may find this volume less readable than other Harvard Health Talks which have preceded it.

J. B.

The Anaemias. By JANET M. VAUGHAN. 2nd ed. 309 pp. Illus. $4.50. (*Oxford University Press, London, 1936.*)

The second edition of this excellent monograph is longer than the first, and four coloured plates as well as five other illustrations have been added. It may be recommended without reservation as giving an accurate account of present knowledge and current opinion regarding the anaemias, insofar as this is possible in a field which is the subject of so much active investigation. Only the hemoglobinurias seem to have received inadequate consideration. The material is conveniently arranged so that desired information can be readily found. There is a useful, selected bibliography.

M. M. W.

A Manual of Pharmacology. By TORALD SOLLMANN. 5th ed. 1190 pp. $7.50. (*W. B. Saunders Co., Philadelphia, 1936.*)

The early editions of this text were noted for the completeness with which they included even minute details of pharmacological interest.

Unfortunately, the present edition, although completely reset, fails to maintain the unique character of the original edition. The omission of many recent pharmacological advances is in marked contrast to the inclusion of manifold detailed data concerning earlier work.

A. G.

BOOKS RECEIVED

Principles and Foibles of Cancer Research in regard to Etiology and Nature. By WILLIAM RIENHOFF, SR. 200 pp. unb. $2.50. Waverly Press, Baltimore, 1936.

Research in Dementia Precox. By NOLAN D. C. LEWIS. 320 pp. $1.50. National Committee for Mental Hygiene, New York, 1936.

Roentgen Interpretation. A Manual for Students and Practitioners. By GEORGE W. HOLMES and HOWARD E. RUGGLES. 5th ed., thoroughly revised. 356 pp. Illus. $5.00. Lea & Febiger, Philadelphia, 1936.

British Masters of Medicine. By SIR D'ARCY POWER. 242 pp. Illus. $3.00. William Wood & Co., Baltimore, 1936.

A Century of Medicine in San Antonio. By PAT IRELAND NIXON. 405 pp. Illus. Privately published by the author, San Antonio, Texas, 1936.

A Textbook of Surgery. By JOHN HOMANS. 4th ed. Entirely reset. 1267 pp. Illus. $8.00. Charles C. Thomas, Springfield, Ill., 1936.

Eugenical Sterilization. By The American Neurological Association, Committee for the Investigation of Eugenical Sterilization. 211 pp. $3.00. The MacMillan Co., New York, 1936.

A Dissertation on the Sensible and Irritable Parts of Animals. By ALBRECHT VON HALLER. [London, J. Nourse, 1755.] Introduction by Owsei Temkin. 49 pp. $1.00. Johns Hopkins Press, Baltimore, 1936.

Snow on Cholera. A reprint of two papers by John Snow. 191 pp. $2.50. The Commonwealth Fund, New York, 1936.

Urological Roentgenology. By MILEY B. WESSON and HOWARD E. RUGGLES. 269 pp. Illus. $5.00. Lea & Febiger, Philadelphia, 1936.

Applied Dietetics. By SANFORD BLUM. 408 pp. $4.75. F. A. Davis Co., Philadelphia, 1936.

Allergic Diseases. By RAY M. BALYEAT. 4th ed. 516 pp. $6.00. F. A. Davis Co., Philadelphia, 1936.

Modern Treatment and Formulary. By EDWARD A. MULLEN. 707 pp. $5.00. F. A. Davis Co., Philadelphia, 1936.

Treatment in Psychiatry. By OSKAR DIETHELM. 476 pp. $4.00. The Macmillan Company, New York, 1936.

Trachoma. By A. F. MACCALLAN. 225 pp. Illus. £1. 1. 0. Butterworth & Co., London, 1936.

The Riddle of Woman. By JOSEPH TENENBAUM. 477 pp. $3.50. Lee Furman, Inc., New York, 1936.

Plastic Surgery of the Nose. By J. EASTMAN SHEEHAN. 2nd ed., 186 pp. Illus. $9.00. Paul B. Hoeber, Inc., New York, 1936.

Skin Diseases in Children. By GEORGE M. MACKEE and ANTHONY C. CIPOLLARO. 345 pp. Illus. $5.50. Paul B. Hoeber, Inc., New York, 1936.

Diseases of the Coronary Arteries and Cardiac Pain. Edited by ROBERT L. LEVY. 445 pp. Illus. $6.00. The Macmillan Co., New York, 1936.

William Withering. The Introduction of Digitalis into Medical Practice. By LOUIS H. RODDIS. 131 pp. Illus. Paul B. Hoeber, Inc., New York, 1936.

Manual for the Medical Services of the Peiping Union Medical College Hospital, 5th ed., 204 pp. $1.50. Peiping, China, 1936.

Les Courants de Haute Fréquence. By GEORGES RONNEAUX. 156 pp. Illus. Unbound, 30 francs. Gauthier-Villars, Paris, 1937.